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Factors Affecting Extrapulmonary Tuberculosis Reinfection in Pulmonary Tuberculosis Patients in Gorontalo City

Muh. Arfah Syam [1], Margaretha Solang [2], Widy Susanti Abdulkadir [3]

[1,2,3]Department of Public Health, Postgraduate, Gorontalo State University, Gorontalo City

ABSTRACT: Tuberculosis is a disease caused by the bacteria *Mycobacterium tuberculosis*. Tuberculosis does not only occur in the lungs, which is called *pulmonary tuberculosis* but can occur outside the lung organs, which is called *extrapulmonary tuberculosis.* Reinfection from *Pulmonary tuberculosis* to *Extrapulmonary tuberculosis* can occur due to several factors. This study aims to determine the factors that can influence the occurrence of reinfection *Extrapulmonary tuberculosis* in *pulmonary tuberculosis sufferers.* Method *Analytical* research with a *cross-sectional approach*. The number of samples was 49 samples of *Pulmonary tuberculosis* sufferers who underwent initial diagnosis at the Anatomical Pathology Laboratory, Prof. Dr. Hi. Aloei Hospital. Saboe Gorontalo City. The results of the study showed that the variables Adherence to treatment (p: 0.047), and BCG Vaccine (p: 0.018) were < α value: 0.05, while the significance value of comorbidity for EPTB Reinfection was (p: 0.991). The conclusion is that adherence to treatment and the BCG vaccine have a significant effect on the incidence of reinfection *Extrapulmonary tuberculosis* (EPTB) in patients with *pulmonary tuberculosis* (PTB), while comorbidities do not have a significant effect on the incidence of reinfection *Extrapulmonary tuberculosis* (EPTB) in patients with *pulmonary tuberculosis* (PTB).

KEYWORDS: Tuberculosis, Extrapulmonary tuberculosis, Pulmonary tuberculosis.

I. INTRODUCTION

Tuberculosis (TB) is a disease that has existed for a long time. Studies of human skeletons show that this disease has affected humans for thousands of years. The cause of this disease was still unknown until March 24, 1882, when Dr. Robert Koch announced the discovery of the bacteria that caused this disease, which was later named *Mycobacterium tuberculosis*. This disease spreads when TB sufferers expel bacteria into the air (for example through coughing). *Tuberculosis* usually attacks the lungs *(Pulmonary tuberculosis)* but can also attack other places *(Extrapulmonary tuberculosis)*. Approximately ninety percent (90%) of TB sufferers are adults and cases occur more frequently in men than women (World Health Organization, 2023).

Qian *et al* ., (2018) mentioned *tuberculosis* (Tb) accompanied by co-infection *human immunodeficiency virus* (HIV), is the main cause of death worldwide. People infected with *Mycobacterium tuberculosis* (Mtb) may have no symptoms (latent TB infection, LTBI) or develop active TB disease. For active TB disease, a small proportion of patients *(19.3-39.3%) suffer from primary extrapulmonary or extrapulmonary* tuberculosis accompanied by lung involvement, while the majority of patients suffer from *pulmonary tuberculosis* (PTB).

World Health Organization, (2023) mentions *tuberculosis* especially targeting *people* with low immune systems such as young children or people with HIV, people with certain conditions such as malnutrition, diabetes or silicosis, and people who smoke or have drug use disorders. Tuberculosis also disproportionately affects people whose health is compromised due to socio-economic circumstances, such as poverty, poor housing, displacement, or imprisonment. TB sufferers are also at higher risk of experiencing mental health disorders. Poor access to health services for this group of people results in continued transmission of tuberculosis as well as worse impacts and stigma, including for those who access health services.

According to The Global TB Report 2020 in the Central TBC Division, (2023) EPTB constitutes 16% of the 7.5 million TB cases reported globally and 19% in Southeast Asia. However, these estimates may be just the tip of the iceberg, as many people remain undiagnosed or unknown. In the last few decades, there has been an increase in EPTB rates in developed countries, in contrast to a decrease in PTB rates. Despite this, EPTB is not usually included in Tb control programs, perhaps because of its lower transmissibility.

Ministry of Health, (2020) stated that the number and rate of *extrapulmonary tuberculosis cases* per 100,000 population continues to increase (7.8 per 100,000 in 2014 to 25.4 per 100,000 in 2018 or 6.4% of all new tuberculosis cases in 2014 to 9.9% in 2018). The proportion of extrapulmonary tuberculosis is high in Papua, which is a province with a high prevalence of HIV and childhood TB. In contrast, the proportion of extrapulmonary tuberculosis cases is low in Sulawesi and other small islands.

In 2022, based on preliminary data surveys that researchers obtained at the Gorontalo Provincial Health Service, it was reported that 5 (five) people had confirmed cases of EPTB. Similar to data from the Gorontalo City Health Service, only 1 (one) person was reported to have suffered from EPTB. This data is inversely proportional to the data of patients who underwent an examination to confirm the diagnosis of EPTB at the Anatomical Pathology Laboratory Installation at the Regional Hospital. Prof. DR. Dr. Hi. Aloe Saboe Gorontalo City, a brief interview with the doctor in charge of the laboratory (Anatomical Pathology Specialist) revealed that in 2022 there will be approximately 100 cases. In 2023, for the January – October period, 57 PTB-EPTB sufferers were reported. The initial survey was conducted in August – October 2023 through short interviews with PTB – EPTB sufferers at the Anatomical Pathology Laboratory Installation at RSUD.Prof.DR.dr.Hi.Aloei Saboe Gorontalo City numbered 7 (seven) people, it was found that all respondents did not know what EPTB was. All they know is that tuberculosis in general is PTB. Before carrying out an examination, the doctor always asks about treatment history, compliance with treatment, and the respondent's medical history as well as smoking behavior in adult category patients.

EPTB case in Gorontalo City is like an iceberg phenomenon, where only a little is visible on the surface but much is not visible below the surface or invisible. This research needs to be carried out in the hope that knowledge of the wider community and health workers about EPTB disease can be better through education and information. Tracing and investigating contact history is necessary to suppress the spread of tuberculosis infection. Motivation and education for both direct sufferers and their families are very necessary so that the recovery rate increases. Smoking habits greatly influence the success of treatment for EPTB sufferers. By examining the influence of PTB sufferers' smoking behavior, it can be seen whether the spread of tuberculosis germs is passive or massive to organs outside the lungs. Socioeconomic status is a factor that is interrelated with efforts to treat TB sufferers. By knowing how significant the influence of SES is, the government can strive for government programs in the tuberculosis elimination program and health disparities will be reduced. By knowing the comorbidities of EPTB sufferers, tuberculosis treatment efforts will be more focused. Information and administration of the BCG vaccine can prevent the spread and transmission of EPTB. Based on the background above, researchers want to look at the factors *that influence Extra Pulmonary* Tuberculosis reinfection *in Pulmonary Tuberculosis* sufferers *in Gorontalo* City.

II. RESEARCH METHODS

A. Research methods

This research uses the *Analytical Survey method* which aims to analyze the factors that influence reinfection *of extrapulmonary tuberculosis* in patients *Pulmonary tuberculosis.* The research design used was *a Cross-Sectional Study.*

B. Population and Sample

The population in this study were all *pulmonary tuberculosis patients* with reinfection Extrapulmonary *tuberculosis* at the Anatomy Pathology Laboratory Installation at Prof. RSUD. DR. Dr. Hi. Aloei Saboe Kot a Gorontalo. Based on initial data on reinfected PTB patients *with Extrapulmonary tuberculosis* 72 people carried out histocytopathological examinations for the period January – December 2023.

a. Inclusion Criteria

1) Patients diagnosed with reinfection *Pulmonary tuberculosis – Extrapulmonary tuberculosis* in the PA Laboratory.
2) Age (12 – 60 years).

b. Exclusion Criteria

1) *Pulmonary tuberculosis - Extrapulmonary Tuberculosis* patients in the category of children.
2) Not willing to fill out the questionnaire

The sampling method used in this research is *Purposive Sampling*, the sample taken is a selected sample based on certain criteria. The selection criteria are: The samples in this study are listed in the inclusion and exclusion criteria.

C. Data collection technique

Research instruments are tools used to collect research data in the form of questionnaires (lists of statements), observation formulas, and other formulas related to data recording and so on (Notoatmodjo, 2018). The instrument used in this research is a questionnaire sheet, namely several written questions that are used to obtain information from respondents in terms of their personality or things that respondents know in the research (Arikunto, 2018). The questionnaire sheet is prepared in such a way as to suit the needs of the variables to be studied to obtain information that is relevant to the research objectives. Before being

used as a data collection tool, the questionnaire used in this research had gone through the questionnaire testing stage which included testing the validity and reliability of the research data.

III. RESULTS AND DISCUSSION

A. The Influence of Treatment Adherence to the Incidence of Reinfection *Extrapulmonary Tuberculosis*

Table 1. Distribution of Treatment Compliance Variables on REPTB Incidents

Obedience Get treatment					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Obedient	5	10.2	10.2	10.2
	Simply Obedient	37	75.5	75.5	85.7
	Not obey	7	14.3	14.3	100.0
	Total	49	100.0	100.0	

Source: SPSS data processing results in version 26.0, 2024

In the research, it was found that the results of the analysis influenced adherence to treatment and reinfection of *Extrapulmonary tuberculosis* (EPTB), categorized as compliant, moderately compliant, and non-compliant. Respondents who are at risk of experiencing reinfection are in the group of respondents with a fairly obedient level of compliance. The proportion of not sufficiently compliant was 37 respondents (75.5 %), 7 respondents (14.3%) were not compliant and 5 respondents (10.2%) were compliant. The significance value of Treatment Adherence to EPTB Reinfection (p: 0.047). So compliance with treatment for *pulmonary tuberculosis sufferers* influences the incidence of reinfection *Extrapulmonary tuberculosis*.

The results of this research are in line with Jangid *et al,* (2018), non-adherence to treatment is often caused by a lack of knowledge or understanding about the disease and its treatment. On the other hand, better knowledge about TB can increase acceptance of control measures resulting in a reduction in the spread of the disease. By educating patients and dispelling their misconceptions, patient compliance with therapy and the spread of the disease will likely improve.

According to Setiani *et al.,* (2022), compliance can be defined as a patient's behavior in carrying out instructions or treatment methods recommended by a doctor or medical personnel. Low compliance can increase disease risk or prolong disease To worsen the patient's condition, low patient compliance is also one of the factors that causes failure in the healing process.

The main causes of patient non-compliance are forgetting to take medication, being away from home, side effects from medication, not being able to go to a health facility on the appointment date, and being hospitalized. According to Jorstad, *et al* (2018) Many EPTB patients, who present to the main referral hospital in Zanzibar, experience long delays in starting treatment, especially patients with TB lymphadenitis. Health system delays are a major contributor to total delays. Improvement in self-rated health after treatment implies that timely treatment has the potential to reduce morbidity and economic losses for patients.

B. The Influence of Comorbidities on the Incidence of Reinfection *Extrapulmonary Tuberculosis*

Table 2. Distribution of Comorbid Variables on the Incidence of REPTB

Comorbid					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	There isn't any	42	85.7	85.7	85.7
	There is	7	14.3	14.3	100.0
	Total	49	100.0	100.0	

Source: SPSS data processing results in version 26.0, 2024.

In the research, it was found that the results of the analysis of the influence of economic comorbidities on reinfection *Extrapulmonary tuberculosis* (EPTB), were categorized as present and absent. Respondents who are at risk of reinfection are in the group of respondents without comorbidities. The proportion of no comorbidities was 42 respondents (85.7%), and there were 7 respondents (14.3%). The significance value of comorbidities for EPTB reinfection (p: 0.991). So comorbidities in *pulmonary tuberculosis sufferers* do not influence the incidence of reinfection *Extrapulmonary tuberculosis*.

The results of this study are in line with Bhattacharya *et al.,* (2020) that accompanying or comorbid diseases were present in 53.17% of patients, of which diabetes mellitus (DM) (26.58%) and hypertension (17.34%) were the most common. Comorbid

conditions were significantly higher in PTB than EPTB (51 of 83 vs. 41 of 90, p<0.05). The most common comorbidities found in most respondents were diabetes mellitus and hypertension.

The World Health Organization, (2022) stated that in 2020, the five main risk factors for TB related to health history, namely diabetes, human immunodeficiency virus (HIV), disorders due to alcohol use, smoking, and malnutrition contributed 4.5 million (45%) sufferers of new and relapsed TB globally. These health-related risk factors are considered comorbidities if a person also has TB. TB sufferers often experience other comorbidities including mental disorders and viral hepatitis. All of these comorbid conditions are associated with poorer TB treatment outcomes and poor socioeconomic outcomes.

C. Effect of BCG Vaccine on Reinfection Events *Extrapulmonary tuberculosis*

Table 3. Distribution of BCG Vaccine Variables on REPTB Incidence

BCG vaccine					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Never	9	18.4	18.4	18.4
	Once	40	81.6	81.6	100.0
	Total	49	100.0	100.0	

Source: *SPSS data processing results in version 26.0, 2024.*

In the research, it was found that the results of the analysis of the influence of economic comorbidities on reinfection *Extrapulmonary tuberculosis* (EPTB), were categorized as ever and never. Respondents who were at risk of experiencing reinfection were in the never-respondent group. The proportion of those who had ever received the BCG vaccine was 40 respondents (81.6%), and 9 respondents who had never received it (18.4%). The significance value of the BCG vaccine against EPTB reinfection (p: 0.018). So the BCG vaccine status in *pulmonary tuberculosis sufferers* influences the incidence of reinfection *Extrapulmonary tuberculosis*.

These findings are in line with Barreto *et al.,* (2011) hypothesis that BCG vaccination offers higher efficacy at a low prevalence of non-tuberculosis mycobacteria (NTMb), and suggest that revaccination with BCG provides weak protection in certain subgroups. Houda Ben *et al.,* (2018) in their research stated that a systematic review and meta-analysis studying the current evidence for BCG against tuberculosis shows that the efficacy of BCG vaccination is usually high, especially against serious forms of EPTB such as meningeal and miliary tuberculosis. The studies reviewed also showed a high level of protection against death in EPTB patients. When BCG vaccination is only given to infants or children after rigorous screening for tuberculin sensitivity, efficacy against EPTB is higher compared with adults. BCG vaccination protects against EPTB for up to 10 years, but highly variable and often very low efficacy against PTB in adults is reported. Therefore, even with the high coverage currently achieved, BCG is unlikely to have a major impact on transmission.

According to Helwig *et al.,* (2018) the word "vaccine" comes from the Latin Variolae vaccinae (cowpox), which was shown by Edward Jenner in 1798 to prevent smallpox in humans. Today the term 'vaccine' applies to all biological preparations, produced from living organisms, that increase immunity to disease and prevent (prophylactic vaccines) or, in some cases, treat disease (therapeutic vaccines). The vaccine is given in liquid form, either by injection, orally, or intranasally.

BCG revaccination is still used in several countries where tuberculosis is endemic. To date, there is little evidence to suggest that BCG revaccination provides very limited additional protection, although there is no information on whether protection depends on the site and age of revaccination, or whether protection increases with time since vaccination.

IV. CONCLUSION

From the results of the research and analysis in this study, it can be concluded that adherence to treatment and the BCG vaccine has a significant effect on the incidence of reinfection *Extrapulmonary tuberculosis* (EPTB) in patients with *pulmonary tuberculosis* (PTB), while comorbidities do not have a significant effect on the incidence of reinfection *Extrapulmonary tuberculosis* (EPTB) in *pulmonary tuberculosis* (PTB) sufferers in Gorontalo City.

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