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# Prevalence and risk factors of latent tuberculosis infection in adolescent in Islamic boarding schools

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**Abstract**--Latent tuberculosis infection (LTI) is an obstacle in eradicating pulmonary tuberculosis. 5-10% people with LTI will develop into active tuberculosis (TB) in the first 5 years after the first TB infection. Islamic boarding schools are a highly potential area in increasing LTI incidents in adolescents. Existing studies are mostly focused on reporting LTI in the general population. To determine the prevalence and risk factors of LTI in adolescents in islamic boarding schools in Bangkalan Madura. A cross sectional study was conducted at the Islamic Boarding School Bangkalan Madura in January 2022 using a random sampling technique. The IGRA examination using the QIArearch QuantiFERON TB tool. The risk factors analyzed include age, gender, nutritional status, TB contact history, duration of stay in Islamic boarding schools and level of knowledge. The data obtained were further analyzed using chi-square and logistic regression test. A total of 100 subjects were examined by IGRA resulting in 30 positive subjects consisting of 30.3% male and 29.9% female. TB contact history (OR 5.167; 95% CI = 1.831-14.567; p=0.002) and level of knowledge about TB (OR 0.019; 95% CI = 0.005-0.069; p<0.05) are significantly related to the incidence of LTI in adolescents in islamic boarding schools. There were 30 subjects with positive IGRA results from 100 examined subjects. TB contact history and level of knowledge about TB are risk factors for the incidence of LTI in adolescents in Islamic boarding schools in Bangkalan Madura.

**Keywords**--Tuberculosis, latent tuberculosis, adolescents, Islamic boarding schools, risk factors.

## Introduction

Latent tuberculosis infection (LTI) is an obstacle in eradicating pulmonary tuberculosis. Studies reported 5-10% people with LTI will develop into active tuberculosis (TB) within 5 years after the first infection. Adolescents with LTI have a higher risk in the disease's transmission, hence causing a disturbance in their academic and social communities. LTI cases are commonly discovered in areas with inadequate sanitation and high-density residential areas such as Islamic boarding schools and dormitories, particularly if the students pay less attention to health and hygiene in preventing tuberculosis transmission.

In 2011, World Health Organization (WHO) reported 10-12% global TB cases consist of adolescents, with 250.000 cases of TB in adolescents and 100.000 deaths caused by TB. There were 1.7 billions global individuals with LTI in 2014, with 35% of the estimated cases coming from Southeast Asia. In 2020, WHO considers Indonesia as one of the High Burden Countries for TB.

LTI prevention can be managed by controlling risk factors and leading a healthy and hygienic lifestyle in a clean environment and surroundings, which particularly needs to be done in Islamic boarding schools. Few studies have been conducted concerning LTI in adolescents in Islamic boarding schools despite a higher risk of LTI in this community. This study is conducted to determine the prevalence and risk factors of LTI in adolescents in Islamic boarding schools in Bangkalan Madura.

## Materials and Methods

Students aged 10-18 years old residing in Islamic boarding schools in Bangkalan Madura were chosen as participants. Samples were randomly taken in the mentioned population and were later examined for Interferon Gamma Release Assay (IGRA). The inclusion criteria of this study are 10 to 18 year-old adolescents with positive IGRA registered as students in Islamic boarding schools in Bangkalan Madura. The given informed consents were agreed and signed by the students' parents and/or legal guardians. The exclusion criteria of this study are patients with history of prior tuberculosis infection and/or have undergone prior tuberculosis treatment. IGRA was conducted using QIArearch QuantiFERON-TB. This study was approved by the Clinical Research Unit of Faculty of Medicine Airlangga University Number 267/EC/KEPK/FKUA/2021. The obtained data was processed using a descriptive analysis method in SPSS 21. Bivariate analysis with Chi-square test was conducted to determine the relation between risk factors included in independent variables to the dependent variables. Variables proven to be significant ( $p < 0,05$ ) were analyzed using logistic regression test to determine the significance of these variables to the dependent variables.

## Result

A total of 100 adolescents aged 10-18 years old were included in this study. The characteristics of all participants are reported in Table 1.

Table 1 Characteristics of participants

Variable	Quantity n (%)
Gender	
Male	33 (33%)
Female	67 (67%)
Age	
≤ 15 years old	32 (32%)
>15 years old	68 (68%)
Nutritional status	
Underweight	0 (0%)
Normal	48 (48%)
Overweight/Obese	52 (52%)
TB contact history	
Yes	20 (20%)
No	80 (80%)
Duration of residence in islamic boarding schools	
< 1 year	42 (42%)
≥ 1 year	58 (58%)
Level of knowledge about TB	71 (71%)
Good	29
Poor	29%)

The participants consist of 33 (33%) male adolescents and 67 (67%) female adolescents, with 32 (32%) participants aged ≤ 15 years old and 68 (68%) participants aged >15 years old. A total of 52 (52%) adolescents are obese and 48 (48%) adolescents are at normal weight, with no underweight or malnourished participants. TB contact history was found positive in 20 (20%) adolescents. There were 42 (42%) adolescents residing in Islamic boarding schools for <1 year and 58 (58%) adolescents residing for ≥ 1 year. There were 71 (71%) adolescents with good knowledge about TB and 29 (29%) adolescents with poor knowledge about TB.

Table 2. Bivariate analysis of LTI risk factors in adolescents in Islamic boarding schools in Bangkalan Madura

Variable	n (%) IGRA (+)	n (%) IGRA (-)	OR	CI 95%	p value
Gender					
Male	10 (30,3%)	23	1,022	0,412-2,534	0,963
Female	(69,7%)				
Age	20 (29,9%)	47	0,876	0,347-2,212	0,779
≤ 15 years old	(70,1%)				
>15 years old	9 (30%)	23			
	(32,9%)				
	21 (70%)	47			
	(67,1%)				

Nutritional status					
Normal	6 (12,5%)	42	0,167	0,060-0,460	<0,05*
Overweight/Obese	(87,5%) 24 (46,7%) (53,8%)	28			
TB contact history					
Yes	12 (60%)	8	5,167	1,831-14,567	0,002*
No	(40%) 18 (22,5%) (77,5%)	62			
Duration of residence					
< 1 year	16 (38,1%)	26	1,934	0,814-4,597	0,100
≥ 1 year	(61,9%)				
Level of knowledge about TB					
Good	14 (24,1%)	44	0,019	0,005-0,069	<0,05*
Poor	(75,9%) 6 (8,5%) (91,5%) 24 (82,8%) (17,2%)	65 5			

\*p<0,05 statistically significant

Bivariate analysis using chi-square test to analyze the relation between age, gender, nutritional status, TB contact history, duration of residence in Islamic boarding schools, and level of knowledge about TB to LTI incidence in adolescents in Islamic boarding schools. Nutritional status ( $p<0,05$ ), TB contact history ( $p=0,002$ ), and level of knowledge about TB ( $p<0,05$ ) are significantly related to LTI incidence in adolescents in Islamic boarding schools. Analysis results are reported in Table 2.

Table 3. Multivariate analysis of LTI risk factors in adolescents in Islamic boarding schools

Variable	Exp (B)	CI 95%	p value
Gender	0,336	0,068-1,654	0,180
Age	2,123	0,734-6,143	0,165
Nutritional status	0,347	0,085-1,423	0,142
TB contact history	6,489	1,236-34,072	0,027*
Duration of residence	0,806	0,192-3,379	0,769
Level of knowledge about TB	0,011	0,002-0,066	<0,05*

\*p<0,05 statistically significant

The multivariate analysis on Table 3 reported that the p value of TB contact history and knowledge concerning LTI is <0,05, therefore indicating that both risk factors are equally significant in affecting LTI incidence in adolescents in islamic boarding schools.

## Discussion

A total of 100 adolescents aged 10-18 years old were included in this study, consisting of 33 male adolescents and 67 female adolescents. A positive IGRA result was found on 30% of the participants (30 students). In India, 5,434 students were tested using tuberculin skin test (TST) and 18% of them came out LTI positive. Another study in 2015 using TST involving 258 students in China managed to detect 46 cases of LTI. This study involved 68 adolescents aged >15 years old and 32 adolescents aged ≤ 15 years old. A study in 2015 conducted in Houston, the United States of America, concerning IGRA test for LTI detection reported 16 positive IGRA in 415 students in two schools aged 15 years old on average.

There were 10 male students and 20 female students with positive IGRA results. In 2012, it was reported that the male to female ratio of tuberculosis cases in the world is 1.9:1, meanwhile in New York, the male to female tuberculosis mortality ratio is 2:1. A study in Europe revealed the ratio of TB cases in male and female students did not have a significant difference, however, TB incidence increased in older male children. This might be related to changes in children's sexual hormones and lifestyle. The study contradicts a research using clinical signs of TB as a parameter of infection conducted in boarding schools in Garut, West Java, that reported males have risks of being infected by TB with an odds ratio of 1.9 compared to females. However, the study only used clinical signs as a parameter for TB infection.

This study does not show any significance between age to risk of LTI infection. This statement corresponds with a study by Ma, et. al. in 2015 that reported no significance between age and LTI incidence in 258 adolescents in a boarding school in China. However, this statement contradicts a research by Dorje, et. al. published in 2018 that reported adolescents aged 14-17 had risks of being infected by TB. Another study using IGRA stated that age 15 to 16 years old is a significant risk factor of LTI infection.

This study shows that nutritional status is significantly related to LTI incidence in adolescents in Islamic boarding schools. There were normal-weight and overweight/obese adolescents without any underweight or malnourished adolescents. Adolescents with obesity have a higher risk of TB infection compared to well-nourished adolescents. Nutrition is crucial in enhancing innate immunity and Th1 for protection against tuberculosis. The existing theory stated that severely malnourished children are 8.88 times higher in risk of TB infection compared to children with normal nutritional status and 32.87 times compared to mildly malnourished children, and significantly higher in risk compared to overweight children. A case-control study in India had previously stated that inadequacy of nutrition is a significant risk factor ( $p=0,001$ ) of TB incidence, with 11,55 higher risk of TB infection (95% CI=3.33-40.15). A 7-year cohort study conducted in adults in Taiwan claimed that there was a complex non-linear relation between obesity, diabetes, and LTI due to the increase of metabolic and cardiac markers.

TB contact history is a significant risk factor of LTI incidence in this study. Adolescents having contact with adult TB patients, have a higher risk of TB infection. A history of close contact with TB patients whose clinical signs include coughing will increase the risk and amount of droplets inhaled into alveoli and induce specific cellular immunity inhibiting the growth of *Mycobacterium tuberculosis* (MTb) without eradicating it, thus keeping it as inactive granuloma that is not able to be eliminated by the immune system. This inactive granuloma may reactivate once the host's immune system is no longer able to keep the granuloma intact. Children and adolescents aged 5-14 years old with a history of close contact with adult TB patients are almost three times more likely to be infected with tuberculosis compared to  $\geq 15$  years-old children. Another study claimed that TB reactivation is 15 times more likely in those who are infected for the first time (2 years). Children less than 5 years old with a history of close contact with adult TB patients have a risk of 56% to develop into active TB in 5 months meanwhile 5-14 year-old children will have a risk of 27.6%.

This study shows that duration of residence in Islamic boarding schools is not a significant risk factor of LTI incidence in adolescents in Islamic boarding schools. A case report in Bandung, West Java, reported a 15-year-old adolescent infected with TB resided in an Islamic boarding school for 3 years prior to TB diagnosis. A study reported LTI prevalence detected in boarding schools in Tibet is four times higher in the first year of study compared to LTI prevalence in India and South Africa in 2016. The study stated that new LTI cases in adolescents  $< 15$  years old in the first year of the study in Tibet is 5 to 8 times higher compared to India, China, and globally. Heterogeneity of LTI prevalence in boarding schools in Tibet is affected by various factors, including prior LTI cases, boarding school's density, ventilation in boarding schools, along with health facility and accessibility. A prior study in Israel claimed 6 LTI cases in 398 adolescents aged 15 to 18 years old in boarding schools in Israel after one year of study detected using TST.

Level of knowledge about TB in this study is a significant risk factor of LTI incidence in adolescents in Islamic boarding schools. One of the significant factors in TB prevention is knowledge about TB because a broader knowledge about TB, including knowing the signs and symptoms, will raise more awareness of TB, therefore TB transmission and LTI have a higher chance to be prevented. Another study claimed that the risk of LTI in people with poor knowledge of TB is 3.5 times higher than people with good knowledge of TB. Knowledge about TB is not commonly taught in Indonesia, especially in Islamic boarding schools. Islamic boarding schools in Indonesia are focused on its teachings of religious studies above any other study topics, hence the limited opportunity for the students to obtain more information regarding health.

The use of IGRA as an LTI diagnostic tool in this study is advantageous because it has higher sensitivity, it can obtain results within 24 to 48 hours, and follow up is not needed to conclude the test results. Failure to fulfill and interpret the questionnaire correctly is disadvantageous in this study, thus may create bias in obtaining information. Researchers met difficulties in finding studies about LTI because of the limited number of LTI studies in adolescents. The nutritional status that is stated to be significantly related to LTI in this study does not correspond with the existing theory.

## Conclusion

There were 30 subjects with positive IGRA test results from 100 examined subjects. TB contact history and knowledge about TB are risk factors for the incidence of LTI in adolescents in Islamic boarding schools in Bangkalan Madura.

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