



Research article

Risk factors for *Tuberculosis* in children at labuang baji hospital and center for community pulmonary health Makassar in 2023

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Received - 23-11-2023, Revised - 11-02-2024, Accepted - 12-03-2024 (DD-MM-YYYY)

Refer This Article

Mughnizah, A Arsunan Arsin, Ansariadi, Ridwan A, Apik Indarty M, Hasnawaty A, 2024. Risk factors for *Tuberculosis* in children at labuang baji hospital and center for community pulmonary health Makassar in 2024. Journal of medical pharmaceutical and allied sciences, V 13 - I 2, Pages - 6422 – 6428. Doi: <https://doi.org/10.55522/jmpas.V13I2.5930>.

ABSTRACT

Efforts to achieve the Sustainable Development Goals (SDGs) include eradicating the global tuberculosis (TB) epidemic by 2030. In 2020, the global TB incidence rate stood at 121 per 100,000 people, with 1.1 million children succumbing to the disease worldwide.

Indonesia alone recorded 42,187 pediatric TB cases in 2021, emphasizing the urgency of addressing this public health concern. A recent observational study in Makassar City focused on children aged 0-14, revealing 380 cases in 2022, notably concentrated in Labuang Baji Regional Hospital, Tajuddin Chalid Hospital, and Community Center for Lung Health Makassar. Developing countries, where children under 15 constitute 40-50% of the population, witness around 500,000 pediatric TB cases annually, leading to severe morbidity and mortality, especially in those under 14. May to July 2023, researchers conducted a case-control study involving 114 children. The study revealed that malnutrition (with an odds ratio of 2.614 and a 95% confidence interval of 1.133-6.085) and a history of TB contact (with an odds ratio of 7.84 and a 95% confidence interval of 2.932-22.319) emerged as noteworthy risk factors for pediatric TB. Notably, economic status, residential density, BCG vaccination status, and exposure to smokers showed no significant impact on the prevalence of the disease. The study advocates consistent screening of adult TB patients' family contacts to trace potential cases in children. Future research should explore the feasibility of TB transmission among children. Tackling malnutrition and strengthening contact tracing initiatives are imperative to curbing pediatric TB, aligning with global goals for a TB-free world by 2030.

Keywords: Children *Tuberculosis*, Malnutrition, History of contact with *Tuberculosis*.

INTRODUCTION

Ending the global *Tuberculosis* (TB) epidemic by 2030 is one of the aims agreed upon by all nations in the Sustainable Development Goals (SDGs) agenda. In 2020, the global TB incidence rate was 121 per 100,000 people. In 2020, the ten nations with the highest proportion of TB incidences (74%) in the globe are India (24%), Indonesia (11%), and the Philippines (8,3%)^[1]. In terms of children's tuberculosis infections, WHO estimates show that 1.1 million children worldwide died from the disease in 2020^[2].

In Indonesia, the number of TB cases discovered in 2020 was 351,936 cases, a reduction from the total number of tuberculosis cases discovered in 2019, which was 568,987 cases. Meanwhile, the number of cases of child TB in Indonesia in 2021 was 42,187, with 23,674 cases aged 0-4 years and 18,513 cases aged 5-14 years^[3].

In developing countries, children under the age of 15 account for 40-50% of the overall population, and TB affects around 500,000 children worldwide each year^[4]. From 2010 to 2018, the proportion of Children TB patients among all cases treated in Indonesia fluctuated

from 9.4% to 11%. This statistic remains within the typical range for the proportion of children tuberculosis cases among all TB cases. Child TB cases are anticipated to be approximately 10-15% based on modeling^[5]. Even while it is still within acceptable limits, TB cases in children may grow if not addressed effectively.

According to the 2021 South Sulawesi Provincial Health Service Profile, there were 386 child TB cases, with Makassar City having the most, with 138 instances. According to statistics from the South Sulawesi Province Health Office's SITB, the number of cases in Makassar City in 2022 WAS 380, with the three biggest instances being at Labuang Baji Regional Hospital, Tajuddin Chalid Hospital, and Center for Community Pulmonary Health Makassar.

Tuberculosis is a major source of morbidity and mortality, particularly in newborns and young children, since TB infection can advance quickly to illness, particularly in this population globally. Tuberculosis in children reflects the disease's prevalence in adults as well as the community's current rate of transmission^[6].

METHODS

Research Design

This study was conducted in Makassar, namely at the Labuang Baji Regional Hospital and the Center for Community Pulmonary Health Makassar. In 2022, the hospitals with the most children TB cases were Labuang Baji Hospital, Tajuddin Chalid Hospital, and Center for Community Pulmonary Health Makassar . The study was conducted between May and July of 2023. This study was a case control study using an analytical observational approach.

Research Sample

The children in this study were 14-year-olds who were diagnosed with children tuberculosis using a score system (>6) and had positive tuberculin test results and were treated at Labuang Baji Regional Hospital and Center for Community Pulmonary Health Makassar between May and July 2023. This study's overall sample size was 114 children. There were 57 controls and 57 cases. The sample size calculation formula was used to determine the sample size for hypothesis testing on the odds ratio ^[7]. Children diagnosed with *Tuberculosis* and currently undergoing treatment (but not in the end phases of treatment) were eligible for inclusion in the case group. Children with illnesses of the respiratory tract (non-TB) who were not having TB screening were included in the control group.

Data Collection and Data Analysis

Data was collected through direct interviews with respondents' parents using questionnaires, as well as by reviewing medical record data housed at the hospital (TB Registry) utilizing the Android-based Kobo Toolbox. Stata Version 14 was used for data analysis. The odds ratio test for bivariate analysis and the logistic regression test for multivariate analysis were used to evaluate relationships between variables with a 95% confidence level (=0.05%).

RESULTS

Source : Primary Data, 2023

According to Table 1, 83.3% of the total 114 respondents were from Labuang Baji Hospital, the majority of the respondents were male (59.65%), and the majority of the respondents were 5 years old (57.89%).

Table 1: General Characteristics of Respondents

Characteristics	Case		Control		Total	
	n=57	%	n=57	%	n=114	%
Research Location						
Labuang Baji Hospital	9	15.79	10	17.54	19	16.67
Center for Community Pulmonary Health Makassar	48	84.21	47	82.46	95	83.33
Gender						
Male	33	57.89	35	61.40	68	59.65
Female	24	42.11	22	38.60	46	40.35
Age Group						
≤ 1 year	4	7.02	9	15.79	13	11.40
1 – 4 years 11 months	29	50.88	24	42.11	53	46.49
5 – 14 years	24	42.11	24	42.11	48	42.11

Source: Primary Data, 2023

According to Table 2, the majority of the respondents' fathers' last education in both the case and control groups was high school (44.74%), whereas the majority of the respondents' mothers' last education was college/university (48.25%). In the job category, the respondent's father worked as a private employee (52.63%), while the respondent's mother worked as a housewife (52.63%). Respondents' income and spending factors ranged from IDR 2,000,000 to IDR 5,000,000, the majority (60.53%) shared a house with smokers

(57.89%), and the majority (83.33%) had a dwelling area of 36 m2. Source: Primary Data, 2023.

Based on the data in Table 3, the Odds Ratio (OR) value for the nutritional status variable was 7.84 (95% CI: 1.133 - 6.085) with the lower and upper limit (LL-UL) values not including the value 1, implying that children with poor nutritional status were 2,614 times more likely to be infected with tuberculosis than children with good nutritional status.

Table 2: Characteristics of Respondent Families

Characteristics	Cases		Control		Total	
	n=57	%	n=57	%	n=114	%
Father's Education						
Elementary-Junior High School	10	17.55	9	15.81	19	16.66
Senior High School	20	35.09	31	54.39	51	44.74
College/University	27	47.37	17	29.82	44	38.6
Mother's Education						
Elementary-Junior High School	6	10.52	10	17.55	16	14.03
Senior High School	22	38.60	21	36.84	43	37.72
College/University	29	50.88	26	45.61	55	48.25
Father's Occupation						
Civil Servants/ Indonesian Army/ Police	5	8.77	6	10.53	11	9.65
Private Sector Employee	32	56.14	28	49.12	60	52.63
Entrepreneurship, and others	20	35.09	23	40.35	43	37.72
Mother's Occupation						
None	37	64.91	38	66.67	75	65.79
Civil Servants/ Indonesian Army/ Police	2	3.51	8	14.04	10	8.77
Private Sector Employee	13	22.81	7	12.28	20	17.54
Entrepreneurship, and others	5	8.77	4	7.02	9	7.89
Parent's Income						
≤ Rp 2.000.000	7	12.28	7	12.28	14	12.28
Rp 2.000.000 – Rp 5.000.000	36	63.16	33	57.89	69	60.53
≥ Rp 5.000.000	14	24.56	17	29.82	31	27.19
Parent's Expense						
≤ Rp 2.000.000	13	22.81	16	28.07	29	25.44
Rp 2.000.000 – Rp 5.000.000	38	66.67	31	54.39	69	60.53
≥ Rp 5.000.000	6	10.53	10	17.54	16	14.04
Living with a smoker						
Yes	34	59.65	32	56.14	66	57.89
No	23	40.35	25	43.86	48	42.11
House Size						
< 36 m2	3	5.26	16	28.07	19	16.67
≥ 36 m2	54	94.74	41	71.93	95	83.33

Table 3: Results of Bivariate Analysis of Risk Factors for Children TB Incidents Based on Research Variables at Center for Community Pulmonary Health Makassar and Labuang Baji Regional Hospital in 2023

Variable	Cases		Control		P value	OR	95 % CI
	n	%	n	%			
Malnutrition							
Yes	30	52.63	17	29.82	0.0134	2.614	1.133 - 6.085
No	27	47.37	40	70.18			
Contact History							
Yes	32	56.14	8	14.04	0.000	7.84	2.932 - 22.319
No	25	43.86	49	85.96			
Low Economic Status							
Yes	7	12,28	7	12,28	1.000	1	0.276 - 3.613
No	50	87.71	50	87.71			
BCG Immunization Status							
No	3	5.26	3	5.26	1.000	1	0.1281- 7.802
Yes	54	94.74	54	94.74			
Residential Density							
Yes	10	17.54	17	29.82	0.123	0.500	0.183 - 1.319
No	47	82.46	40	70.18			
Contact with Smokers							
Yes	34	59.65	32	56.14	0.704	1.154	0.513 - 2.598
No	23	40.35	25	43.86			

The Odds Ratio (OR) for the contact history variable was 7,84 (95% CI: 2.932 - 22.319), with the lower and upper limit (LL-UL) values excluding the value 1. This demonstrated that a history of

interaction with tuberculosis patients is a substantial risk factor for the occurrence of tuberculosis in children. Children who have had interaction with adult tuberculosis patients have a 7.84 times greater

chance of contracting tuberculosis than children who have had no contact with TB patients.

Based on the data in Table 3, the value of Odds Ratio (OR) = 1 (95% CI: 0.216 - 4.625) was derived in the economic status variable, with the lower and upper limit (LL-UL) values containing the value 1. As a result, it may be stated that children from low-income families were not a risk factor for the occurrence of childhood tuberculosis.

Based on the data in Table 3, the Odds Ratio (OR) value for the BCG immunization status variable was 1 (95% CI: 0.1281- 7.802) with the lower and upper limit (LL-UL) values including the value 1. So, there was no relationship between BCG immunization status and the incidence of tuberculosis in children.

Based on statistical testing, the residential density variable had an Odds Ratio (OR) value of 0.500 (95% CI: 0.183 - 1.319) with the lowest and upper limit (LL-UL) values included the value 1. The OR value of 1 indicated that residential density 0.5 times the risk of the incidence of tuberculosis in children but indicating that it was not statistically significant.

The results in Table 3 revealed an Odds Ratio (OR) test of 1.154 (95% CI: 0.513 - 2.598) in the risk variable for history of contact with smokers, with the lower limit and upper limit (LL-UL) values containing a value of 1 indicating contact with smokers was a minor risk factor for the occurrence of TB in children. As a result, children who lived with smokers had a 1,154-fold increased chance of contracting TB, despite this risk factor was statistically insignificant.

Source : Primary Data, 2023

The data from the multivariate analysis in Table 4 showed that the variables nutritional status and contact history were statistically significant variables with lower and upper CI values not including one and a p value of 0.05, indicating that these two variables met the criteria for analysis. The stepwise technique was the second stage of multivariate analysis. This second technique demonstrated that contact history had the greatest effect on the occurrence of TB in children.

Multivariate Analysis

The chance of children TB incidence from characteristics that had been established to be important risk factors for children tuberculosis is as follows:

$$p = \frac{1}{(1 + e^{-(coef\ constant + coef\ riwayat\ kontak + coef\ status\ gizi)})}$$

$$p = \frac{1}{(1 + e^{-(1,2622 + 2,2558 + 1,2641)})}$$

$$p = \frac{1}{(1 + e^{-(0,9053)})}$$

$$p = 0,9053$$

$$p = 90,53\%$$

This indicated that a kid aged 0-14 years who was underweight and had a history of interaction with TB patients had a 90.53% chance of contracting TB.

Table 4: Multivariate Analysis Result

Variable	Model 1			Model II		
	OR	95% CI	p	AOR	95% CI	p
Malnutrition						
Yes	2.614	1.211-5.644	0.014	3.540	1.453-8.623	0.005
No						
Contact History						
Yes	7.840	3.149-19.522	0.000	9.543	3.604-25.271	0.000
No						
Low Economic Status						
Yes	1	0.326-3.060	1.000			
No						
BCG Immunization Status						
No	1	0.193-5.177	1.000			
Yes						
Residential Density						
Yes	0.501	0.206-1.216	0.127			
No						
Contact with Smokers						
Yes	1.155	0.549-2.431	0.704			
NO						

DISCUSSION

According to the findings of this study, 67 respondents (58.77%) had high nutritional status, whereas the remaining 47 (41.23%) had low nutritional condition. Thirty (52.63%) of the 57 Children TB patients had low nutritional status^[8]. Bivariate analysis revealed that children with poor nutritional status were 2,614 times more likely to contract TB than children with high nutritional condition.

In contrast, a 2018 study on 240 Children TB patients at the Purwokerto Community Lung Health Center discovered that nutritional status and BCG immunization status did not have a significant effect on the occurrence of TB in children, whereas child age and people's knowledge did. The knowledge of parents about tuberculosis and intimate interaction with adult TB patients had a

major impact on the incidence of TB in children ^[9]. The knowledge factor of parents is vital in TB prevention. Abdul Madjid's research discovered that educating women with TB knowledge through interventions has a very beneficial effect on discovering TB patients near them ^[10].

Nutritional conditions may affect people of all ages, but newborns and children are the most vulnerable since they require so many nutrients to sustain their general growth and development. The majority of children with low nutritional status were under the age of five (70.21%). A child's immune system is relatively weak at birth and progressively improves throughout the first five years of life. Children are also less able to prevent illness transmission through the blood until the age of five, and this capacity gradually increases as they get older. A child's dietary quality has a positive influence on the spread of sickness in his lungs. Stunted nutritional toddlers are more likely to get tuberculosis than normal nutritional toddlers ^[11].

The connection between malnutrition, infection, and growth and development is complicated. The impact of consumption patterns, nutrition, and illness on nutritional status in children vary and are determined by disease ecology, age, consumption patterns, and the type of food ingested. There are two possible outcomes for the two's connection. (1) low nutritional status impairs body immunity and diminishes resistance to infection; and (2) exposure to infectious illnesses can induce lack of appetite, such as anorexia, malabsorption of nutrients, and increased energy metabolism of other nutrient. The presence of adult tuberculosis patients in one household makes other family members vulnerable to the illness. Mycobacterium Tuberculosis bacteria are very tiny and very infectious, spreading by coughing, sneezing, or chatting together, putting family members who often come into touch with patients prone to infection, particularly in infants and toddlers ^[12]. If the symptoms in adult TB patients are not too severe, such as a cough that has been present for more than two weeks and causes the sufferer not to see a doctor, and the patient's unwillingness to see a doctor despite the fact that the sufferer has the potential to infect others, the people around him are vulnerable. infected.

According to the findings of the multivariate analysis, contact history was a risk factor that impacted the incidence of tuberculosis in children by 9.54 times. This study's findings were consistent with prior research, which found that 57% of children who had household contact with adult TB patients with rifampicin resistance were infected with the disease. Drug-resistant instances in adult patients with tuberculosis provide a new challenge to TB control operations ^[13]. This might have an influence on child tuberculosis cases. A case control study conducted in Ambon City in 2019 by Ivy Lawalata revealed that the risk of tuberculosis in children with a history of home contact was 31 times higher than in children with no history of household contact. Because TB reactivation does not occur

in children, each new case demonstrates the transfer of infection from a source of transmission in the community. It is always a family member or someone close to the children who is the source ^[14]. Because of the high risk implied by this contact history, urgent screening of TB patients' relatives or contact history tracing in children TB cases is required.

Socioeconomic status is directly tied to job and type of work, and the amount of family income is also related to location of housing, family living patterns, and food habits. Socioeconomic status has an impact on a person's level of knowledge and attitude in preventing TB. Research conducted by Abdul Madjid shows that knowledge and attitudes influence the incidence of Tuberculosis in the Mandar tribe population ^[15].

According to the theoretical framework utilized in this study, economic status was a risk factor for children tuberculosis. However, the study's findings revealed that economic position was unrelated to the occurrence of tuberculosis in children (OR=1). In this study, 87.71% (50 individuals) of respondents in the case and control groups had sufficient economic level or had a low risk of incident TB in children. The poverty line standard in South Sulawesi Province was employed by researchers in this study, where the average poverty line per poor home was IDR 1,954,038/poor household/month^[23]. The results of this study were in accordance with studies completed by Yustikarini (2015) revealing that there was no significant association between socio-economic position and the incidence of children TB. In contrast to study done in Nigeria in 2018, poor socio-economic level (79.2%) was a risk factor related with pulmonary TB in children ^[16].

Vaccination with BCG (Bacillus Calmette Guerin) is required for all newborns and children under the age of four months. In several countries, BCG is used alongside If a baby aged 4 months or older is detected, BCG is not administered; instead, a tuberculin test must be performed; if negative, BCG can be given; if positive, a TB diagnostic process must be performed, followed by a TB treatment regimen. Thus, BCG vaccination is still necessary to avert problems and ensure that children grow and develop normally, free of secondary tuberculosis.

Because of the minimal risk of Mycobacterium tuberculosis infection, inconsistent vaccination efficacy against adult pulmonary TB, and potential interference with tuberculin skin test reactivity, BCG is typically not advised for use in the United States. The BCG vaccination should only be considered for persons who satisfy specified requirements and visit a tuberculosis expert.

The findings of this study revealed that there was no link between BCG vaccination status and the incidence of tuberculosis in children (OR=1). In this study, 94.74% of respondents in the control and case groups had received the BCG vaccination. The existence of BCG scars on one of the respondent's arms demonstrated this

vaccination status. Respondents who have not got the BCG vaccine are LBW, which means that the BCG vaccine cannot be administered to normal-weight newborns. As a result, the number of respondents in the control and case groups who got the BCG vaccine was larger than the number of respondents who did not get the BCG vaccine. A history of BCG vaccination was shown to be a protective (neutral) risk factor for the incidence of TB in children in Ambon (2019) (OR = 0.101 with 95% CI LL-UP 0.010-1.024). Giving the BCG vaccination to a newborn will result in a stronger immunological response, particularly a cellular immune response rather than a humoral immune response. Because the immune response is intimately tied to the body's ability to fight disease, study findings indicate that vaccination will boost the body's resistance against TB.

In 2011, a study on children TB risk factors in Bangladesh proposed providing the BCG vaccination to children at a young age since it provided 75% protection for 15 years [17].

One of the factors that might enhance the incidence of pulmonary tuberculosis is residential density. Overcrowding in a residence can have an impact on health since it can result in disease transmission from one person to another.

According to the findings of this study, residential density 0.5 times the risk of the incidence of tuberculosis in children. In this study, 82.46% of respondents in the case group had a residential density of 9m² or higher in their home. In the control group, 70% of responders satisfied the population density standards. Thus, respondents with TB and those without TB had a larger density of residents who fulfilled the requirements than those with pulmonary tuberculosis, who had a higher density of residents who did not match the standards. This demonstrated that the great majority of respondents' homes were acceptable.

This contrasted with Amelia Rizki's 2018 research at the Kaluku Bodoa Community Health Center in Makassar City, which found a significant link between residential density and the prevalence of pulmonary tuberculosis (Chi-Square test p value = 0.027 (p0.05). Other research indicates that residential density, as one of several environmental variables, had a link with and is a risk factor for TB in the Tinambung Community Health Center region of West Sulawesi. The more crowded the residence, the simpler it is for infections to spread, especially those transmitted via the air, such as tuberculosis (TB). If a family member with TB with positive BTA coughs accidentally, the tuberculosis bacteria will linger in the air for roughly 2 hours, potentially transferring the disease to relatives who have not been exposed to M. Tuberculosis bacteria [18].

In this study, contact with smokers is defined as having family or relatives who smoke and live in the same area as the respondent. As a result, in both the control and case groups, the majority of respondents, 57.89%, lived in the same house as smokers.

The bivariate analysis yielded an Odds Ratio (OR) test of 1.154 (95% CI: 0.513 - 2.598) with lower and upper limit (LL-UL) values including a value of 1 indicating that contact with smokers was a risk factor, which was not significant for the incidence of childhood *Tuberculosis*. As a result, children who lived with smokers had a 1,154-fold increased chance of contracting TB, despite this risk factor was statistically insignificant.

The respondent's family's smoking habits were as follows: 64.6% smoked at home and 35.38% smoked outside the house. The family of respondents who smoke at home was made up of 64.29% who smoked 11-20 cigarettes per day, 21.43% who smoked 10 cigarettes per day, and the remaining 14.29% who smoked 21 cigarettes per day. As a result, several of the respondent's relatives smoked moderately to heavily.

According to research conducted in Ambon that linked the smoking habits of parents of children suffering from tuberculosis, OR = 0.536 with (CI 95% LL-UP 0.189-1.521) indicating an OR value 1, parental smoking behavior was not a protective factor (neutral) on the incidence of tuberculosis in children [19].

Children who had domestic contact with smokers had a 7.094 times chance of acquiring TB (OR=7.094, 95% CI: 2128-23648), according to a research done in Pakistan. Children who were exposed to cigarette smoke were at a greater risk of having active pulmonary tuberculosis (PTB) shortly after infection (aOR 5.4, 95% CI 2.4-11.9), and this risk was substantially larger in children aged 0-9 years than in children aged 10 year. Teenage smoking is a risk factor for tuberculosis in young adulthood.

Cigarette smoke includes about 4,000 compounds that are harmful, mutagenic, and carcinogenic in various ways. Cigarette smoke emits a variety of components in both the cellular and extracellular compartments, including water-soluble particles and gasses. Many compounds are carcinogenic and poisonous to cells, but tar and nicotine have been found to be immunosuppressive by changing the host's innate immune response and making the host more susceptible to infection. The larger the concentrations of tar and nicotine, the greater the impact on the immune system.

Cigarette smoke damages the lung defense mechanism, affects lung function, damages the airway mucosa, increases airway resistance, and causes pulmonary blood vessels to leak easily. This makes the lungs more vulnerable if exposed to *Mycobacterium tuberculosis* [20]

CONCLUSION

The risk variables that impacted the incidence of tuberculosis in children included nutritional status (2.6 times) and contact history (7.84 times). A child aged 0-14 years who was underweight and had a history of interaction with TB patients had a 90.53% chance of contracting tuberculosis.

Research limitations

Concerning the study sample, numerous respondents in the control group became cases toward the conclusion of the research period, therefore, the researcher needed more time to hunt for respondents in the control group again. Researchers were unable to distinguish whether low nutritional status preceded the occurrence prior to being infected with TB in the respondent or whether respondents had poor nutritional status as a result of the impacts of being infected with TB.

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