

## Contextual Effect of Village on the Incidence of Tuberculosis in Children in Surakarta, Central Java: A Multilevel Analysis Evidence

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### ABSTRACT

**Background:** Indonesia is in the second place with the highest burden of tuberculosis (TB) in the world. Childhood is a period of rapid growth that requires efforts to maintain children's health. At the time the child still has a low immune system making it vulnerable to a disease including TB. The problem of TB in children requires better attention in child TB control programs. This study aimed to analyze the contextual influence of villages on the incidence of TB in children.

**Subjects and Method:** This was a case-control study conducted in 25 villages in Surakarta, Central Java, from August to September 2019. A sample of 200 children aged 0 to 18 years was selected by fixed disease sampling. The dependent variable was the incidence of TB in children. The independent variables were birth weight, BCG immunization, exclusive breastfeeding, nutritional status, parental income, home sanitation, exposure to cigarette smoke, family history of TB, and contextual effect of village. Data on TB were obtained from medical record in Surakarta community health center. The other data was collected by questionnaire. The data was analyzed by multilevel multiple logistic regression with Stata 13.

**Results:** The risk of TB in children increased poor house sanitation (OR= 6.70; 95% CI= 1.14 to 39.27; p= 0.035), high exposure to cigarette smoke (OR= 6.71; 95% CI= 1.09 to 41.25; p= 0.040), and family history of TB (OR= 6.01; 95% CI= 1.36 to 26.39; p= 0.018). The risk of TB in children decreased with normal birth weight ( $\geq 2500$  g) (OR= 0.12; 95% CI= 0.02 to 0.60; p= 0.009), BCG immunization (OR= 0.17; 95% CI= 0.04 to 0.64; p= 0.009), exclusive breastfeeding (OR= 0.08; 95% CI= 0.01 to 0.57; p= 0.011), good nutritional status (OR= 0.11; 95% CI= 0.02 to 0.66; p= 0.016), and parental income  $\geq$  Rp 1,802,700 (OR= 0.07; 95% CI= 0.01 to 0.37; p= 0.002). Village had strong contextual effect on the risk of TB in children with intra-class correlation (ICC)= 29.24%.

**Conclusion:** The risk of TB in children increases poor house sanitation, high exposure to cigarette smoke, and family history of TB. The risk of TB in children decreases with birth weight  $\geq 2500$  g, BCG immunization, exclusive breastfeeding, good nutritional status, and high parental income. Village has strong contextual effect on the risk of TB in children.

**Keywords:** Tuberculosis, risk factors, children aged 0-18 years, multilevel analysis.

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### BACKGROUND

Childhood is a period of rapid growth and development, so there is a need for efforts to maintain children's health aimed at forming healthy, intelligent and quality future generations and to reduce child mortality. Efforts to maintain children's health from

the time the fetus was still in the womb until the age of 18 years. Children still have a low immune system so they are vulnerable to a disease including tuberculosis (TB) (Ministry of Heal, 2019).

TB is still the tenth highest cause of death in the world, until now TB is still a

top priority in the world and is one of the goals in the SDGs (Sustainability Defense Goals) (World Health Organization, 2016.) Five countries with the highest TB incidence are India, Indonesia, China, the Philippines and Pakistan. Indonesia ranks second with the highest TB burden in the world. Trends in incident TB cases that have not been reached and detected, even if detected and treated but have not been reported (Ministry of Health, 2019).

The 2013 Basic Health Research Data (Riskesdas) states that pulmonary TB has been diagnosed in the <1 year age group by 2%, the 1 to 4 year age group by 4%, the 5-18 year age group by 3%, whereas in the age group of people other adults also showed a similar prevalence of 3%. The results of the 2013 Riskesdas study also showed that there was a recent health problem related to the incidence of pulmonary TB that had attacked the age group of children (Ministry of health, 2015).

The problem of TB in children requires better attention in TB control programs. The main challenges in pediatric TB control programs are a tendency to overdiagnosis or under-diagnosis of pediatric TB cases, inadequate case management, case tracking has not been routinely carried out and under-reporting of pediatric TB patients. Risk factors for childhood TB events in Indonesia are related to child factors (nutritional status, birth weight, history of exclusive breastfeeding and immunization status), parental factors (education, employment, income and knowledge), environmental factors and contact with adult TB sufferers (Aziz, 2018).

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## SUBJECTS AND METHOD

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### 1. Study Design

This was an observational analytic method with a case-control study approach. The study was conducted in 25 villages spread

in each working area of UPT Puskesmas Surakarta. It was conducted August-September 2019.

### 2. Population and Sample

The population in this study were children aged 0-18 years amounting to 200 subjects. Sampling in this study uses fixed disease sampling with a ratio of 1:3 of children who live in 25 villages spread in each working area of UPT Puskesmas in Surakarta City.

### 3. Variables of Study

The dependent variable was the incidence of TB in children. The independent variables were birth weight, BCG immunization, history of exclusive breastfeeding, nutritional status, parental income, home sanitation, exposure to cigarette smoke, family history of TB, and contextual village.

### 4. Operational Definition of Variables

**Incidence of TB children aged 0-18 years** were children aged 0-18 years who are diagnosed with TB by a doctor or health worker at the moment or based on the notes in the medical record book (Medical Record). The measuring instrument used was the medical record. The data scale was categorical with grouping data 1 = tuberculosis, 0 = no tuberculosis.

**Birth weight** was the baby's weight at birth regardless of gestational age and is expressed in grams. The measuring tool was a baby scale. The scale of the data was continuous, but for analytical purposes the data were converted into a dichotomy by grouping data 0 = low (<2,500 g), 1 = normal ( $\geq 2,500$  g).

**BCG immunization** was a vaccine given to protect themselves against TB on a schedule that is appropriate to their age, based on the immunization schedule recommended by the Indonesian Ministry of Health. The measuring instrument used was a questionnaire. The data scale was categorical with data grouping 0 = no BCG immunization, 1 = BCG immunization.

**History of exclusive breastfeeding** was only breastfeeding from birth until the age of 6 months without providing additional food and or drinks except drugs or vaccines with medical indications. The measuring instrument was a questionnaire. The scale of the data was categorical with grouping of data 0 = no exclusive breastfeeding, 1 = exclusive breastfeeding.

**Nutritional Status** was a state of nutritional status of children which is calculated based on anthropometric measurements (BMI/age) using the WHO anthropometric program. The measuring instrument was a stampede scale. The scale of the data was continuous, but for analytical purposes, the data was converted into a dichotomy by grouping data 0 = malnutrition, 1 = good nutrition.

**Parental education** was the highest level of formal schooling achieved by structured and tiered parents, assessed based on the last diploma obtained. basic or low education (elementary, junior high, equivalent) and further or higher education (high school, academy, university). Based on the National Education System Law No. 20 of 2003. Questionnaires was the measurement tools (checklist). The way to measure it was with interview. The scale of the data was categorical with data grouping 0 = Low (elementary, junior high, equivalent), 1 = high (high school, academy, university).

**Parent income** was the average amount of income each month for the past 6 months that the family has received in the form of honorarium, rent including subsidies or benefits and expressed in rupiah. The measuring instrument was a questionnaire. The scale of the data was continuous, then for the data analysis, data were converted into categorical data by grouping data as 0 = low (< minimum wage Rp. 1,802,700), 1 = high ( $\geq$  minimum wage (Rp. 1,802,700).

**House sanitation** was a sanitation condition of a house inside a house that consists of air humidity, house ventilation, temperature of the house, natural lighting and density of residents. The measuring tool was an observation checklist. The scale of the data was continuous before then changed into categorical for the purpose of analysis by grouping the data as 0 = not meeting healthy requirements (score <20), 1 = meeting healthy requirements (score  $\geq$ 20).

**Exposure to cigarette smoke** was exposure to cigarette smoke at home that comes from family members who smoke who live in the same household with children. The measuring instrument was a questionnaire. The data scale was categorical with the grouping of data as 0 = there are families who smoke, 1 = no families who smoke.

**Family TB history** was a family that has been diagnosed with TB by a doctor or health worker at this time or who is based on a record in a medical record book. The measuring instrument was a medical record. The data scale was categorical with grouping data 0 = there is a family history of TB, 1 = there is no family history of TB.

**The economic status of the village** was the economic status of the village is the economic capacity of a village which is reflected in the percentage of poor people in the village. The measurement tool was a questionnaire containing data on the economic status of the village determined by the Regional Planning and Development Agency (BAPPEDA) based on data from the Central Statistics Agency (BPS) which was the result of data analysis of the National Socio-Economic Survey (Susenas).

## 5. Data Analysis

Univariate analysis was carried out to describe the general picture of each variable studied. Bivariate analysis was performed to describe the effect of one independent variable on a dependent variable. Multiva-

riate analysis was carried out to describe the effect of more than one independent variable on one dependent variable. The independent variables include socio-economic, environmental and risk factors, namely birth weight, BCG immunization, history of exclusive breastfeeding, nutritional status, parents' income, home sanitation, exposure to cigarette smoke, family history of TB. Meanwhile, the dependent variable in this study is the incidence of TB in children.

### 6. Research Ethics

This study was conducted based on research ethics, namely informed consent, ano-

nymity, confidentiality, and ethical eligibility. Ethics permission in this study was obtained from the Health Research Ethics Commission Dr. Moewardi Hospital, Surakarta, Indonesia, No. 1023 / VIII / HREC / 2019.

## RESULTS

### 1. Sample Characteristics

The categorical data sample description explains the continuous data of each study variable including birth weight, nutritional status, home sanitation, and family income shown by the table 1.

**Table 1. Description of characteristics of continuous data samples**

Variable	n	Mean	SD	Min.	Max.
Birth weight (g)	200	2865.75	414.455	2000	4200
Nutritional Status (BMI)	200	20.80	2.538	15.5	28.3
House Sanitation	200	21.25	1.818	17	25
Family Income (Rp)	200	2,763,500	2,153,580	900,000	15,000,000

**Table 2. Description of the characteristics of the categorical data sample**

Characteristics	Frequency (n)	percentage (%)
<b>Children age</b>		
2 to <12 months	39	19.5
12 to 59 months	37	18.5
5 to 18 year	124	62.0
<b>Gender</b>		
Male	93	46.5
Female	107	53.5
<b>Parents age</b>		
<20 years	3	1.5
20 to 35 years	76	38.0
≥35 years	121	60.5
<b>Parents education</b>		
Primary school	26	13.0
Junior high school	62	31.0
Senior high school	84	42.0
College	28	14.0

### 2. Univariate Analysis

Table 2 showed most of child were at age 5-18 years (62%). As many as 53.5% children were female. Most of the parental aged was >35 years old (60.5%). As many as 42% parents had education ≥Senior high school.

### 3. Bivariate Analysis

Bivariate analysis in this study was performed using Chi Square analysis. Table 3 shows that children with normal birth

weight (OR= 0.06; p<0.001), BCG immunization (OR= 0.13; p<0.001), exclusive breastfeeding (OR= 0.14; p<0.001), good nutritional status (OR= 0.17; p<0.001), high parental income (OR= 0.24; p<0.001) decreased the risk of TB. Unhealthy home sanitation (OR= 5.81; p <0.001), cigarette smoke exposure (OR= 22.65; p<0.001), and family with history of TB (OR= 13.34; p <0.001) increased the risk of TB.

**Table 3. Chi Square test factors that influence the incidence of TB in children**

Independent variables	TB status				OR	95% CI		p
	Non TB		TB			Lower limit	Upper limit	
	n	%	n	%				
<b>Birth weight</b>								
Low (<2,500 g)	15	32.61	31	67.39	0.06	0.02	0.15	<0.001
Normal (≥2,500 g)	135	87.66	19	12.34				
<b>BCG Immunization</b>								
No	8	34.78	15	14.9	0.13	0.04	0.36	<0.001
Yes	142	80.23	35	19.77				
<b>Exclusive Breastfeeding</b>								
No	27	47.37	30	52.63	0.14	0.06	0.31	<0.001
Yes	123	86.01	20	13.99				
<b>Nutritional Status</b>								
Poor (<18.5)	19	45.24	23	54.76	0.17	0.07	0.37	<0.001
Good (≥18.5)	131	82.91	27	17.09				
<b>Parents Income</b>								
Low (< Rp. 1,802,700)	46	58.97	32	41.03	0.24	0.11	0.51	<0.001
High (≥ Rp. 1,802,700)	104	85.25	18	14.75				
<b>House sanitation</b>								
Healthy	13	29.55	31	70.45	5.81	2.23	11.39	<0.001
Unhealthy	137	87.82	19	12.18				
<b>Smoke exposure</b>								
Yes	32	42.67	43	57.33	22.65	8.84	64.16	<0.001
No	118	94.40	7	5.60				
<b>Family History of TB</b>								
Yes	9	28.12	23	71.88	13.34	5.17	35.92	<0.001
No	141	83.93	27	16.07				

#### 4. Multivariate Analysis

The multivariate analysis method used was a multilevel multiple logistic regression analysis which was carried out using the

Stata 13. The multivariate analysis explained the effect of more than one independent variable on one dependent variable.

**Table 4. Multilevel multiple logistic regression analysis of socioeconomic, environmental and risk factors that influence TB in children**

Independent Variables	OR	95% CI		p
		Lower limit	Upper Limit	
<b>Fixed Effect</b>				
Birth weight (≥2,500 gram)	0.12	0.02	0.60	0.009
BCG immunization (yes)	0.17	0.04	0.64	0.009
Exclusive breastfeeding history (yes)	0.08	0.01	0.57	0.011
Nutritional status (good)	0.11	0.02	0.66	0.016
Parents income (≥ Rp. 1,802,700)	0.07	0.01	0.37	0.002
House sanitation (unhealthy)	6.70	1.14	39.27	0.035
Smoke exposre (yes)	6.71	1.09	41.25	0.040
Family history of TB (yes)	6.01	1.36	26.39	0.018
<b>Random Effect</b>				
Village				
Var (Constata)	1.36	0.09	19.58	
N observation	200			
LR test vs. Logistic Regression, p=0.013				
Intraclass Correlation (ICC)= 29.24%				

Table 4 shows there are socioeconomic, environmental and risk factors such as birth weight, BCG immunization, history of exclusive breastfeeding, nutritional status, parental income, home sanitation, exposure to cigarette smoke and family history of TB. The risk of TB incidence in children decreases with normal birth weight (OR= 0.12; p= 0.009), BCG immunization (OR= 0.17; p= 0.009), exclusive breastfeeding (OR= 0.08; p= 0.011), good nutritional status (OR= 0.11; p= 0.016) and high parental income (OR= 0.07; p= 0.002). The risk of pediatric TB incidence increased with unhealthy home sanitation (OR= 6.70; p= 0.035), exposure to cigarette smoke (OR= 6.71; p= 0.040) and family history of TB (OR= 6.01; p= 0.018). There was a contextual effect on the risk of the incidence of TB in children (ICC= 29.24%).

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## DISCUSSION

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### 1. The effect of birth weight on the risk of TB incidence in children

The results showed that children who had normal birth weight had a lower risk of developing TB, which was 0.12 times compared to children who had low birth weight.

Children with low birth weight tend to easily experience decreased respiratory function and have an increased risk of chronic respiratory disease during childhood (Lee et al., 2003). The results of the study of Xin et al. (2019), also states that children with low birth weight will experience impaired immune function. The more severe growth retardation experienced by the fetus, the more severe the damage to lung structure and function, as well as immunocompetent disorders and such damage will persist throughout childhood. Low birth weight is related to immaturity in the respiratory organs, this will influence the initial adaptation process in response to various exposures (Florescu et al., 2015).

### 2. The effects of BCG immunization on the risk of TB in children

The results showed that children who received BCG immunization had a lower risk of developing TB, which was 0.17 times compared to children who did not get BCG immunization.

Children who do not get BCG vaccination according to their age based on recommendations from the Indonesian Ministry of Health have a higher risk of developing TB compared to children who get BCG vaccination (Hu et al., 2013). Jain et al. (2013) mention this shows that the prevalence of TB among school children can be reduced by strengthening the BCG vaccination under the national immunization program as a strategy for the prevention of active TB (Setiyaningsih et al., 2019).

### 3. The effects of a history of exclusive breastfeeding on the risk of TB incidence in children

The results showed that children who received exclusive breastfeeding had a lower risk of developing TB, which was 0.08 times compared to children who did not get exclusive breastfeeding.

Infants who are exclusively breastfed have a lower risk of developing TB compared to children who are not exclusively breastfed (Hanieh et al., 2015). The content in breast milk that babies drink during exclusive breastfeeding is sufficient for the baby's needs and is in accordance with the baby's health (Fitriani et al., 2019). Breast milk contains immunity to infections including proteins, lysozyme, lactoferrin, immunoglobulins and antibodies against bacteria, viruses, fungi and other pathogens (Aziz, 2018).

Breast milk also increases antibody responses to pathogens in the respiratory tract and increases the immune system. Therefore exclusive breastfeeding reduces child mortality due to various diseases such

as TB and accelerates recovery when sick (Grant et al., 2011)

#### **4. The effect of nutritional status on the risk of TB incidence in children**

The results showed that children with good nutritional status had a lower risk of developing TB, which was 0.11 times compared to children with low nutritional status

Children with malnutrition have a risk of TB of 3.96 times compared with children who have good nutrition (Tekle et al., 2015). Other studies that are in line are research conducted by Grant et al. (2011), it was found that nutritional status has a direct influence on the incidence of TB. Children with poor nutritional status increase the risk of TB.

Malnutrition will cause a decrease in immune capacity to respond to TB infection including impaired granulocyte function, decreased complement function and cause micronutrient deficiencies, disruption of bactericidal phagocytic activity (Ibrahim et al., 2017). Malnutrition in childhood usually involves inadequate intake of protein and calories, with increased micronutrient deficiency (Xin et al., 2019). Protein and micronutrient deficiencies have an impact on hematopoietic and lymphoid organs. Changes related to malnutrition in intestinal microbiota contribute to growth disorders and irregular inflammation and immune function (Jain et al., 2013).

#### **5. The effect of parental income on the risk of TB incidence in children**

The results showed that children with high-income parents have a lower risk of developing TB, which is 0.07 times compared to children with low-income parents.

Children from families with low economic status are more at risk of communicable diseases (Simkovich et al., 2019). Socio-economics is a determining factor for meeting the needs of life, including the quality of sanitation in homes that meet health

requirements (Fitriani et al., 2019). Nutritious food needs and other needs that support the health conditions of family members (Alyahya et al., 2017). Low-income families have limitations in meeting the needs of life that support the whole as well as limited access in preventive and curative efforts (Bai et al., 2018). Low-income families, then the results of their work only to meet their basic daily needs are not optimal (Karim et al., 2012).

#### **6. The effect of home sanitation on the risk of TB incidence in children**

The results showed that children who live at home with sanitation quality that do not meet the healthy requirements have a higher risk of developing TB, which is 6.70 times compared to children who live at home with sanitation quality that meets healthy conditions.

The physical condition of the home environment that does not meet health requirements can support the transmission of diseases and health problems such as TB (Xin et al., 2019). The condition of the physical environment of the house (temperature, natural lighting intensity, type of wall, house floor, ventilation, humidity, occupancy density) is significantly related to the incidence of TB in children (Karim et al., 2012). The government has established regulations regarding housing health requirements, namely Decree of the Minister of Health of the Republic of Indonesia Number 829/MENKES/SK/VII/1999 concerning Housing Health Requirements.

The proportion of houses in Indonesia that met healthy house requirements in 2013 was still low at 24.9%. The findings in this study, about 22% of housing units are houses that do not meet healthy requirements (Surakarta Health Office, 2019). The condition of the physical environment of homes that do not meet health requirements can increase the risk of diseases such

as TB (Ramadhiana et al., 2016). According to Shimeles et al. (2019), home physical environment factors are factors that influence the emergence of lung disease in addition to population factors (gender, age and socio-economic).

Conditions that are not good air humidity is a good medium for the growth of bacteria and viruses that cause diseases including TB (Duarte et al., 2018). Transmission of respiratory diseases is more common in homes that do not meet health requirements because the number of germs is greater than the air that is exchanged (Alyahya et al., 2017).

#### **7. The effect of exposure to cigarette smoke on the risk of TB in children**

The results showed that children who live with family members who smoke have a higher risk for experiencing TB, which is 6.71 times compared to children who live with family members who do not smoke.

Air pollution from cigarette smoke increases the risk of TB occurrence in children (Adesanya et al., 2016). TB is a serious disease problem caused by various factors, one of which is cigarette smoke (Adetifa et al., 2017). Polycyclic Aromatic Hydrocarbons (PAHS) are harmful to human health from the combustion of tobacco products that are usually in the form of cigarette smoke (Environmental Tobacco Smoke / ETS) which is a type of toxic gas (Simkovich et al., 2019).

Cigarette smoke around smokers contains the same toxic and carcinogenic ingredients as smoked by smokers so that the effect on passive smokers is almost the same as active smokers (Koretskaya et al., 2017). Cigarette smoke in addition to carcinogenic effects, can also cause respiratory infections by sulfur dioxide, ammonia and formaldehyde (Patra et al., 2015).

#### **8. The effects of family history of TB on the risk of TB in children**

The results showed that children who lived with family members who had a history of TB had a higher risk of experiencing TB, which was 6.01 times compared to children who lived with family members who did not have a history of TB.

Every TB case in a child is caused by contact with an infected person. Another factor is the number of people living in the same house, the length of time living together, and sharing a room with TB sufferers (Shimeles et al., 2019). Contact with a smear adult TB (+) is a risk factor for TB infection (Adetifa et al., 2017). This difference can be explained by the length of exposure and virulence of *M. tuberculosis* from individuals with TB (Jain et al., 2013). Intimate contact with TB cases is significantly associated with smear-positive TB (Hu et al., 2013). The prevalence among school children can be reduced by increasing the investigation of active contact of TB patients (Patra et al., 2015).

#### **9. Contextual effect of village on the risk of TB in children**

The results of multilevel analysis show that the ICC value = 29.24%, the indicator shows that the condition of each kelurahan area has a contextual influence on the variation in the occurrence of TB in children.

Epidemiological triangle theory explains that the emergence of disease is caused by the influence of host factors (host), causes (agents) and the environment (environment). The environment outside the individual (host) plays an important role in increasing TB in children (Murti, 2016).

Living in poor communities can cause psychosocial stress, which can lead to negative behaviors that can have a negative impact on the health of those around them, such as smoking (Adesanya and Chiao, 2016). The degree of health and poverty of

people in an area affect each other (Ramadhiana et al., 2016). An increase in income does not automatically guarantee poverty reduction unless the health status of the poor is also increased. Health service financing must also get attention so that there is an increase in health status, this will have an impact on increasing the income of its population (Chisti et al., 2015).

The poverty condition also affects the public health behavior of each village/ kelurahan which is also different (Bai et al., 2018). Villages / villages where the majority of people have access to health information tend to have a high awareness of health and will usually influence surrounding residents to jointly care about health (Caesar et al., 2017). Vice versa, residents who live in poor communities mostly have limited access to health information and tend to have a lack of awareness of health, the surrounding environment can be affected and do not care about negative behavior (Cross et al., 2014).

The condition of settlements in each village/kelurahan is different, there are several villages that have a large distance from one house to another, so that the air flow to each house is better than villages/ kelurahan which have narrow and densely populated houses, where sometimes the lighting for passing through the window is often closed by other houses which causes suboptimal humidity and temperature in the house (Murakami et al., 2019).

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#### **AUTHOR CONTRIBUTION**

Dyah Ayu Saputri collected data, did data analysis, and wrote the manuscript. Bhisma Murti did data analysis and interpreted the results of data analysis. Yulia Lanti Retno Dewi formulated the research framework and suggested the materials of nutritional status as determinants of TB incidence in children.

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#### **CONFLICT OF INTEREST**

There is no conflict of interest in this study.

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