Journal of Epidemiology and Public Health (2024), 09(03): 284-299
Masters Program in Public Health, Universitas Sebelas Maret

Research
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Village as Contextual Factors and Other Risk Factors Related with the Incidence of Clinical Tuberculosis in Children in Wonogiri, Central Java: A Multilevel Analysis

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Received: 30 February 2024; Accepted: 2 April 2024; Available online: 16 July 2024

ABSTRACT

Background: Indonesia is in the second rank with the highest burden of tuberculosis (TB) in the world. Childhood is a period of rapid growth, the body still has a low immune system so it is susceptible to disease including tuberculosis in children which requires control efforts. This study aims to analyze the influence of risk factors and village contextual factors on the incidence of TB in children.
Subjects and Method: Case-control study research was conducted in 82 villages in Wonogiri Regency, from November to December 2023. A sample of 200 children aged 0 to 4 years old was selected through fixed disease sampling. The dependent variable of this study was the incidence of TB in children. The independent variables in this study were stunting, contact history, exposure to cigarette smoke, home sanitation, gender, parental education, child age, parental income, BCG immunization status, and village contextual influences. Data on TB disease was obtained from the Tuberculosis Information System Application (SITB) at the Wonogiri District Health Service in 2023. Other data was collected through questionnaires. The data analysis was done through multilevel multiplelogistic regression.
Results: The factors that increased the incidence of TB in children were stunting (OR= 10.94; CI 95%= 2.50 to 47.90; p= 0.001), contact history to TB (OR= 8.37; CI 95%= 1.60 to 43.83; p= 0.012), and exposure to cigarette smoke (OR= 7.36; CI 95%= 1.99 to 27.14; p= 0.003). The reducing factors were healthy sanitation (OR= 0.24; CI 95%= 0.08 to 0.78; p= 0.017), female children (OR= 0.40; CI 95%= 0.15 to 1.05; p= 0.062), and parents with ≥high school education (OR= 0.40; CI 95%= 0.15 to 1.05; p= 0.062). There was no relationship between age (OR= 0.93; CI 95%= 0.13 to 6.23; p= 0.940), parental income (OR= 1.14; CI 95%= 0.40 to 3.25; p= 0.807), and BCG immunization status (OR= 0.12; CI 95%= 0.00 to 105.98; p= 0.550). Village has a contextual influence on the incidence of clinical TB in children (ICC= 52.95%).
Conclusion: The risk of clinical TB in children increased with stunting, a history of TB contact and exposure to cigarette smoke, it decreased with healthy home sanitation, female gender, parents with ≥high school education. There was no relationship between age, parental income, and BCG immunezation status. The village has a contextual effect on the incidence of clinical TB in children.

Keywords: Stunting, contact, income, immunization, sanitation, tuberculosis

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Cite this as:
Hidayati KN, Murti B, Rahardjo SS (2024). Village as Contextual Factors and Other Risk Factors Related with the Incidence of Clinical Tuberculosis in Children in Wonogiri, Central Java: A Multilevel Analysis. J Epidemiol Public Health. 09(03): 284-299. https://doi.org/10.26911/jepublichealth.2024.09.03.02.

BACKGROUND

Tuberculosis (TB) is the second largest cause of death in the world after HIV/AIDS, it is estimated that one-third of the world's population has been infected by Mycobacterium tuberculosis (WHO, 2020). In developing countries, the incidence of TB cases is around 95% and deaths due to TB are 98%. (Indonesian Ministry of Health, 2015). Based on the 2022 Global TB Report, the number of TB cases in Indonesia is 969,000 cases, or 1 person/case every 33 seconds. Indonesia rises to second place in the world with the highest burden of TB cases after India and number 3 is China. The incidence of TB cases is 354/100,000 population in Indonesia. Cases discovered and reported are 443,235 (45.7%). Cases that have not been discovered and reported are 525,765 (54.3%). The number of deaths due to TB is 150,000 (one person every 4 minutes) and the death rate is 55/100,000 population. The coverage of TB patient discovery and treatment is currently still low, namely 67% of SO TB cases and 17% of RO TB cases starting treatment. Of the total 10.6 million cases in 2021, at least 6 million cases are adult males, then 3.4 million cases are adult female and the other TB cases are children, namely 1.2 million cases.

Central Java Province, including Wonogiri Regency, is generally targeting a TC (Treatment Coverage) of 90% in 2023. According to data from the Wonogiri District Health Service, in 2021 the coverage of patient discovery was reported to be around 33%, in 2022 it was 61.11%, while in 2023 to August 2023, the coverage of TB sufferers was reported to be around 71.67%, resulting in a significant increase in TB cases every year (Central Java Provincial Health Office, 2023).

As the incidence of TB in adults increases, the number of children infected with TB and the number of children with TB disease also increases. A child can contract TB infection without clinical symptoms of TB even though there is a positive tuberculin test, so supporting and laboratory examinations are needed, as well as establishing the current diagnosis of TB in children using a scoring system. TB is one of the causes of morbidity and death that often occurs in children. Children are very susceptible to TB infection, especially those who have close contact with bacteriologically confirmed TB patients, and children are also more at risk of suffering from severe TB such as miliary TB and meningitis TB. A child's current TB infection represents a future source of TB disease. The burden of pediatric TB cases in the world cannot be known due to the lack of child-friendly diagnostic tools and inadequate systems for recording and reporting pediatric TB cases, therefore, it is estimated that many children suffer from TB who do not receive proper treatment. In 2017 there were 10 million TB cases in the world and 1.6 million people died from TB. Among these cases, there are 1 million cases of TB in children (0 to 14 years) which is estimated to be around 7.5 million children infected with TB every year. In addition, more than 1 million new cases of childhood TB occur every year (Ministry of Health of the Republic of Indonesia, 2016).

According to WHO (2020), babies and children aged <5 years old have a very high risk of developing TB disease, especially in the first 2 years after infection, babies who have poor nutritional status can develop TB disease within a few weeks. Based on data from the Director General of P2P in 2022, at least 500,000 children in the world suffer from TB every year. Every day 200 children die from TB and 70,000 children die every year from TB. The proportion of childhood TB cases among all TB cases in 2010 was 9.4%, then became 8.5% in 2011 and 8.2% in 2012. From the data per province, it shows

variations in the proportion from 1.8% to 15.9%. This shows that the quality of pediatric TB diagnosis still varies greatly at the provincial level. Child TB cases are grouped into the age groups 0 to 4 years and 5 to 14 years, with the number of cases in the age group of 5 to 14 years higher than the age group of 0 to 4 years old (Ministry of Health of the Republic of Indonesia, 2023).

Data from the Central Java Provincial Health Service (2023) in September showed the number of TB discoveries in children was 201%, an increase from the previous year, 2022, which was 118%. In 2014, the Wonogiri District Health Service reported that 18.2% of TB cases occurred in children aged 0 to 14 years old, but by mid-2015 this had increased to 19.4%. As of September 2023, Wonogiri Regency is in second place with the highest number of TB discoveries in children in Central Java Province at 417% with a total of 480 cases of TB in children from a total of 1,029 cases discovered.

The factor of childhood TB, socio-economic refers to parents' income, which also contributes as a risk factor because children are still responsible for their parents. Meanwhile, the most important risk factor for childhood TB is contact with active TB patients (Wardani and Wahono, 2021). Children who live in the same house as someone with tuberculosis (TB) have a high risk of contracting and suffering from TB. Nutritional status (stunting) in children is related to the child's ability to resist TB disease (Haerana et al., 2021).

The obstacles faced in the pediatric TB control program are the tendency for over-diagnosis or underdiagnosis of pediatric TB cases, inadequate case management, case tracking that has not been carried out routinely, and underreporting of pediatric TB patients. Risk factors for the incidence of TB in children in Indonesia are related to child factors (age, gender, stunting and BCG immunization status), parental factors (education, employment, income and knowledge), environmental factors (home sanitation, exposure to cigarette smoke) and contact with adult TB sufferers (Aziz, 2018).

Based on the explanation above, TB in Indonesia is still a very important problem for TB control measures to be taken, in this case among infants and children. With a multilevel approach, it is hoped that the researchers can determine the influence of various levels so that the researchers can determine the risk of tuberculosis in children. This study aims to analyze risk factors and village contextual factors on the incidence of clinical tuberculosis in children in Wonogiri Regency, Central Java Province.

SUBJECTS AND METHOD

1. Study Design

This research is a case-control study conducted in 82 villages in Wonogiri Regency, Central Java from November to December 2023.

2. Population and Sample

The target population in this study is children aged 0 to 4 years. The sample are 200 children with the classification of 100 children with clinical TB and 100 children without TB. The sampling technique uses fixed disease sampling.

3. Study Variables

The dependent variable is the incidence of clinical childhood TB. The independent variables at level 1 are stunting, contact history, exposure to cigarette smoke, home sanitation, gender, parent education, child age, parent income, and BCG immunization status. The independent variable at level 2 is the Village.

4. Conceptual Definition

Incidence of clinical childhood TB: Children who are declared to be suffering from TB by a doctor or health worker at this time or based on notes in the medical record

book and recorded at the SITB of the Wonogiri District Health Service.

Stunting: TB measurement results and the child's age have been determined using the ePPGM application.

History of contact with TB patients: There is a history of contact between the respondent and TB sufferers in the family, community and respondent's environment.

Exposure to cigarette smoke: Exposure to cigarette smoke at home that comes from smoking family members who live in the same house and the neighborhood where children live.

Home sanitation: The sanitary condition inside the house which consists of aspects of assessing the components of the house (ceilings, walls, floors, bedroom windows, living room windows, ventilation, kitchen smoke holes, and lighting), sanitation facilities (clean water facilities, latrines, wastewater disposal facilities, and waste disposal facilities), as well as the occupant behavior (opening bedroom windows, opening family room windows, cleaning the yard, throwing away feces and throwing away rubbish).

Gender: Gender is the difference in sexual identity between men and women as a determinant of different roles in reproduction.

Parental education: A health care facility carried out by and for the community, guided by relevant officers.

Child's age: The length of life of the child from birth until the time the study was carried out.

Parental income: Income as a result of economic processes or family economic resources received in 1 month.

BCG immunization status: Giving immune injections with BCG immunization to babies as seen from the Healthy Card (KMS) book or examination card.

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

5. Study Instruments

The data collection technique was carried out using a questionnaire as a study instrument. Before the research subjects filled out the questionnaire, the researcher first explained the aims and objectives of the research, explained how to fill out the questionnaire regarding stunting, contact history, exposure to cigarette smoke, home sanitation, gender, parent education, child age, parent income, BCG immunization status.

6. Data Analysis

Univariate analysis is used to describe each dependent and independent variable, that is, data is classified according to data type. Bivariate analysis was carried out to determine variable correlation, the average difference of variables, tested using chi-square. Multivariate analysis was carried out using multiple logistic regression analysis through a multilevel analysis approach.

7. Research Ethics

Research ethics include informed consent, anonymity, confidentiality and ethical feasibility. Ethical feasibility in this study comes from the Health Research Ethics Committee at RSUD Dr. Moewardi with number: 2.105/XI/HREC/2023.

RESULTS

1. Sample Characteristics

Table 1 shows that by using categorical data, 100 respondents (50%) experienced clinical childhood TB, 187 children (93.50%) were

≥1 year old, 112 children (56%) were male, 100 children (50%) had children parents with ≥high school education, 101 children (50.50%) had parents with low income, 43 children (21.50%) experienced stunting, 4 children (2%) did not receive BCG immunization, 32 children (16%) had a history of contact with TB patients BTA+, 155 children (77.50%) are exposed to cigarette smoke, 47 children (23.50%) have houses with healthy sanitation, 31 villages (15.50%) have village economic status in the minus category.

Table 1. Sample characteristics (dichotomous data) (N=200)

Characteristics	Category	Frequency (n)	Percentage (%)
Incidence of TB in Children	No	100	50.0
	Yes	100	50.0
Age	<1 year old	13	6.5
	≥1 year old	187	93.5
Gender	Male	112	56.0
	Female	88	44.0
Parental Education	< High School (low)	100	50.0
	≥ High School (high)	100	50.0
Parental Income	Low	101	50.5
	High	99	49.5
Stunting	No	157	78.5
	Yes	43	21.5
BCG Immunization Status	No	4	2.0
	Yes	196	98.0
History of Contact with TB Patients	None	168	84.0
	Yes	32	16.0
Exposure to Cigarette Smoke	No	45	22.5
	Yes	155	77.5
Home Sanitation	Unhealthy	153	76.5
	Healthy	47	23.5
Village Economic Status	Minus	31	15.5
	Surplus	169	84.5
Incidence of TB in Children	No	100	50.0
	Yes	100	50.0

2. Bivariate Analysis

Bivariate analysis was used to see the influence of the independent variable on the dependent variable which was analyzed using the chi-square test and calculation of the odds ratio (OR) with a confidence level of 95%.

Table 2 shows that children aged <1 year old were 0.84 times more likely to be infected with TB compared to children aged ≥1 year old (OR= 0.84; p= 0.774). Female have a risk of being infected with TB by 0.61 times compared to male, with a relationship that was nearly statistically significant (OR= 0.61; p = 0.088).

There was an influence of parental education on the incidence of TB in children. Children with parents with high school education or above have a risk of being infected with TB by 0.62 times compared to those with <high school education, with a relationship that was statistically close to significant (OR= 0.62; p= 0.090).

Parental income has an influence on the incidence of TB in children. Children with low parental income were 0.59 times more likely to be infected with TB compared to children with high parental income and this was nearly statistically significant (OR= 0.34; p =0.067).

BCG immunization status has no influence on the incidence of TB in children. Children who did not receive BCG immunization were 0.33 times more likely to be infected with TB

compared to children who were given BCG immunization (OR= 0.33; p= 0.336). Stunting has an influence on the incidence of TB in children. Children with stunting have a risk of being infected with TB by 9.02 times compared to those without stunting, and this relationship was statistically significant (OR= 9.20; p= <0.001).

Children with a history of TB contact have a risk of being infected with TB by 8.37 times higher compared to those without a history of TB contact, and this relationship was statistically significant (OR= 8.37; 95% CI= 1.60 to 43.83; p= 0.012). Children with exposure to cigarette smoke have a risk of being infected with TB by 7.36 times higher compared to those without exposure to cigarette smoke, and this relationship was statistically significant (OR= 7.36; CI 95%= 1.99 to 27.14; p= 0.003).

Children who live in homes with good and healthy sanitation have a risk of being infected with TB by 0.24 times compared to poor sanitation, and this relationship was statistically significant (OR= 0.24; 95% CI= 0.08 to 0.78; p= 0.017).

Children who live in villages with surplus economic status have a risk of being infected with TB by 0.19 times compared to those living in minus villages, and this relationship was statistically significant (OR= 0.19; p= 0.001).

Table 2. Bivariate analysis with chi-square test

Independent Variable	TB Incidence in Children				OR	CI (95%)		p
	No		Yes			Lower Limit	Upper Limit	
	n	%	n	%				
Age								
<1 year old	6	46.1	7	53.8	0.84	0.27	2.61	0.774
≥1 year old	94	50.2	187	49.7				
Gender								
Male	50	44.6	62	55.3	0.61	0.35	1.08	0.088
Female	50	56.8	38	43.1				
Parental Education								
< High School (low)	44	44.0	56	56.0	0.62	0.35	1.08	0.090
≥ High School (high)	56	56.0	44	44.0				
Parental Income								
Low	44	43.5	57	56.4	0.59	0.34	1.03	0.067
High	56	56.5	43	43.4				
BCG Immunization								
No	1	25.0	3	75.0	0.33	0.03	3.19	0.336
Yes	99	50.5	97	49.4				
Stunting								
No	94	59.8	63	40.1	9.20	3.67	23.08	<0.001
Yes	6	13.9	37	86.0				
History of Contact with TB Patients								
None	95	56.5	73	43.4	7.02	2.58	19.14	<0.001
Yes	5	15.6	27	84.3				
Exposure to Cigarette Smoke								
No	33	73.3	12	26.6	3.61	1.73	7.52	0.001
Yes	67	43.2	88	56.7				
Home Sanitation								
Unhealthy	67	43.7	86	56.2	0.33	0.16	0.67	0.002

Independent Variable	TB Incidence in Children				OR	CI (95%)		p
	No		Yes			Lower Limit	Upper Limit	
	n	%	n	%				
Healthy	33	70.2	14	29.7				
Village Economic Status								
Minus	6	19.3	25	80.6	0.19	0.75	0.50	0.001
Surplus	94	55.6	75	44.3				

Table 2. Bivariate analysis of fastors related with ServQual

Variable Group	ServQual				OR	p
	Poor		Good			
	N	%	N	%		
Gender						
Male	25	42.3	31	57.6	0.84	0.003
Female	67	43.2	77	56.7		
Age						
<66 years	37	25.7	67	74.3	0.51	0.566
≥66 years	37	38.5	43	61.4		
Number of Elderly Visits						
<6 times	13	18.3	58	81.7	0.11	<0.001
6 times	77	59.7	52	40.3		
Education						
<SHS	60	48.7	63	51.2	4.62	0.142
≥SHS	30	38.9	47	61.1		
Income						
<Rp 2,000,000	49	49.5	50	50.5	0.67	0.261
≥Rp 2,000,000	42	41.6	59	58.4		

3. Multivariate Analysis

Table 3 shows the results of multilevel multiple logistic regression analysis regarding various determinants of risk of TB infection in children. There was an effect of stunting on TB infection in children. Children with stunting have a risk of being infected with TB by 10.94 times higher compared to those without stunting, and this relationship was statistically significant (aOR= 10.94; CI 95%= 2.50 to 47.90; p= 0.001).

There was an effect of a history of contact with adult TB patients on TB infection in children. Children with a history of TB contact have a risk of being infected with TB by 8.37 times higher compared to those without a history of TB contact, and this relationship was statistically significant (aOR= 8.37; CI 95%= 1.60 to 43.83; p= 0.012).

There was an effect of exposure to cigarette smoke on TB infection in children. Children with exposure to cigarette smoke have a risk of being infected with TB by 7.36 times higher compared to those without exposure to cigarette smoke, and this relationship was statistically significant (aOR= 7.36; 95% CI= 1.99 to 27.14; p= 0.003). There was an influence of home sanitation on TB infection in children. Children who live in homes with good sanitation have a risk of being infected with TB 0.24 times lower compared to poor sanitation, and this relationship was statistically significant (aOR= 0.24; CI 95%= 0.08 to 0.78; p= 0.017).

There was an influence of gender on TB infection in children. Females have a risk of being infected with TB by 0.40 times compared to males, and the relationship was

statistically close to significant (aOR= 0.40; 95% CI= 0.15 to 1.05; p= 0.062).

There was an influence of parental education on TB infection in children. Children with parents with a high school education or above have a risk of being infected with TB by 0.39 times lower compared to those with <high school education, with a relationship that was statistically close to significant (aOR= 0.40; 95% CI= 0.15 to 1.05; p= 0.062). Several other variables including child age, parental income, and BCG immunization status did not show a significant relationship with the risk of TB infection.

This multilevel multiple logistic regression analysis models showed a statistically significant difference from the usual multiple logistic regression analysis model (p<0.001). This multilevel analysis showed that the risk of TB infection in children was 52.95% determined by factors at the village level (ICC= 52.95% >8-10%), therefore, the contextual influence of the village shown in the multilevel analysis was very important to note).

Table 3. Multilevel logistic regression analysis of risk factors and village contextual factors

Independent Variables	aOR	CI 95%		p
		Upper Limit	Lower Limit	
Fixed effect				
Age (≥1 year old)	0.93	0.13	6.23	0.940
Gender (female)	0.40	0.15	1.05	0.062
Parental education (≥High School)	0.39	0.13	1.17	0.093
Parental Income (≥Rp 1,968,448.32)	1.14	0.39	3.25	0.807
Stunting (yes)	10.94	2.50	47.90	0.001
Contact history (yes)	8.36	1.60	43.83	0.012
BCG immunization (yes)	0.13	0.00	105.98	0.550
Exposure to cigarette smoke (exposed)	7.36	1.99	27.14	0.003
Home sanitation (healthy)	0.24	0.75	0.77	0.017
Random effect				
Village var (constant)	3.70	1.13	12.09	
n Observation= 200				
n Village= 82				
Log likelihood= -99.59				
LR test= 12.15				
p <0.001				
Intraclass Correlation (ICC) = 52.95 %				

DISCUSSION

1. The effect of stunting on the incidence of clinical TB in children

The results of the study show that children with stunting have a 10.94 times higher risk of developing TB compared to children who are not stunted. Children with poor nutritional problems, one of which is stunting, have a risk of developing TB of 3.96 times compared to children who have good nutrition (Tekle et al., 2015). Children with stunting increase the risk of developing TB. Malnutrition will cause a decrease in immune capacity to respond to TB infection, including impaired granulocyte function, decreased complement function and causes micronutrient deficiencies, disrupted bactericidal phagocytic activity (Ibrahim et al., 2017). Childhood malnutrition usually

involves insufficient protein and calorie intake, with increased micronutrient deficiencies (Xin et al., 2019).

TB is common in children with acute malnutrition. These children may not have typical TB manifestations except malnutrition. Thus, screening for TB should be mandatory in every case of acute malnutrition regardless of presenting symptoms. Furthermore, children usually do not come to hospital due to malnutrition, but they remain in the community until they have other comorbidities (Thakur et al., 2022).

2. The effect of a history of contact with adult TB patients on the incidence of clinical TB in children

The results of the study show that children who live with family members who have a history of TB have a risk of developing TB by 8.37 times higher compared to children who live with family members who do not have a history of TB. Every case of TB in children is caused by contact with an infected person. Other factors are the number of people living in the same house, the length of time they have lived together, and sharing a room with a TB sufferer (Shimeles et al., 2019). Intimate contact with TB cases is significantly associated with positive TB smears (Hu et al., 2013). Prevalence in school children can be reduced by increasing the examination of active contacts of TB sufferers (Patra et al., 2015).

Knowing the source of TB disease transmission can be done through information regarding the history of close contact between children and infectious TB patients. Children are very susceptible to infection through the people around them. The results of research by Brajadenta et al. (2018) and research by Rita and Qibtiyah (2020) both state that a history of contact with TB patients is a risk factor for pulmonary TB in children.

3. The effect of exposure to cigarette smoke on the incidence of clinical TB in children

The results of the study show that children who live with family members who smoke have a higher risk of developing TB by 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 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).

It is possible that children who are exposed to tobacco smoke and indoor air pollution have twice the risk of developing TB compared to children who are not exposed. (Siddalingaiah, 2023). Passive exposure and active exposure to tobacco smoke are associated with TB disease. Smoking is common in most developing countries; therefore, exposure to tobacco smoke may be of great concern because smoking causes the downregulation of macrophage TNF-α in the lungs (Patra et al., 2015).

Cigarette smoke around smokers contains the same toxic and carcinogenic substances as those inhaled by smokers, so the impact on passive smokers is almost the same as on active smokers (Koretskaya et al., 2017). Apart from having a carcinogenic effect, cigarette smoke can also cause respiratory infections due to sulfur dioxide, ammonia, and formaldehyde (Patra et al., 2015). Smoking increases the risk of getting TB. Smoking cessation programs should be promoted as an intervention to reduce the incidence of TB and prevent TB transmission, especially in childhood TB (Koesoemadinata et al., 2020).

4. The effect of home sanitation on the incidence of clinical TB in children

The results of the study show that children who live in homes with sanitation

quality that does not meet healthy requirements have a higher risk of contracting TB by 6.70 times compared to children who live in homes with sanitation quality that meets healthy requirements. The condition of the physical environment of the house (temperature, intensity of natural lighting, type of walls, floor of the house, ventilation, humidity, residential density) is significantly related to the incidence of TB in children (Karim et al., 2012).

According to Shimeles et al. (2019), the physical environment of the home is a factor that influences the incidence of lung disease in addition to population factors (gender, age, and socio-economic). Poor air humidity conditions are a good medium for the growth of bacteria and viruses that cause diseases including tuberculosis (Duarte et al., 2018). Transmission of respiratory diseases occurs more often in homes that do not meet health requirements because the number of germs is greater than the air exchanged (Alyahya et al., 2017).

5. The effect of gender on the incidence of clinical TB in children

The results of the study show that female have a risk of contracting TB 0.40 times compared to male. Research by Nurjana and Tjandrarini (2019) shows that male children are the most dominant risk factor for being 1.6 times more likely to be infected with pulmonary TB than female children. This is probably because boys tend to do more activities inside and outside the home than girls. The opportunity to interact with other TB sufferers is also greater, so the chance of being infected is also higher.

Siddalingaiah et al. (2023) stated that boys compared to girls is not significant. The two included studies by Mumpe-Mwanja et al (2015) and Stevens et al (2014) reported that male has a risk factor, whereas the findings of our study were conflicting. Additionally, very few studies have evaluated gender as a risk factor for childhood TB. Gender can be considered a risk factor only after the child reaches puberty because sexual hormones play an important role in immunological dimorphism (Stival et al., 2014).

6. The effect of parental education on the incidence of clinical TB in children

The results of the study show that children of parents with advanced education or >high school education reduced the risk of childhood TB. Marra et al. (2014) explained that a high level of education affects a person's quality of life because of their knowledge regarding infectious diseases such as tuberculosis. Higher education (b= -2.56; 95% CI= -4.16 to 0.96; p=0.002) reduces and is proven to be a risk factor for tuberculosis (Sayidah et al., 2018).

Judging from the educational background in Wonogiri Regency, there are many residents with basic education (Elementary and Junior High School). Educational background can influence a person's attitudes and behavior. A person's behavior is closely related to the knowledge they have. This knowledge is obtained, among other things, through education. According to Azhar and Perwitasari (2013) education can help to facilitate communication and influence the process of providing and receiving information about health so that it can be easily accepted by family members.

7. The effect of age on the incidence of clinical TB in children

The results of the study showed that children aged 0 years old had a 0.93 times risk of being infected with TB compared to children aged ≥1 year, and the results showed that there was no significant effect between age and the incidence of TB in children. A child's age is known to be a risk factor for pulmonary TB in children. Re-

search conducted by Brajadenta et al. (2018) stated that there was a significant influence between the risk factor of child age (0-5 years old) (p= 0.035) and the incidence of pulmonary TB in children. Research by Patra et al. (2015) also states that children aged 0-5 years old are the most susceptible to pulmonary TB. This is because children aged 0-5 years are still vulnerable to infection. After all, the child's immunity has not yet functioned and developed optimally.

The development of TB infection in children aged 1 to <5 months old is less common than in children aged <12 months old, when this occurs, it mostly causes bronchial or lymph node disease. Airway irritation can cause persistent coughing; with further progression, airway irritation can lead to wheezing and eventually stridor. Extrapulmonary disease is relatively rare in this age group (Stop TB Partnership Childhood TB Subgroup World Health Organization, 2016).

8. The effect of parental income on the incidence of clinical TB in children

The results of the study show that children whose parents have high incomes have a lower risk of developing TB by 0.07 times compared to children whose parents have low incomes. Children who come from families with low economic status are more at risk of contracting infectious diseases (Simkovich et al., 2019). Socioeconomics is a determining factor in fulfilling life's needs, including the quality of sanitation in the home that meets the needs (Fitriani et al., 2019).

The need for nutritious food and other needs that support the health conditions of family members (Alyahya et al., 2017). Low-income families have limitations in fulfilling overall life support needs as well as limited access to preventive and curative efforts (Bai et al., 2018). For families with low incomes, the results of their work just to meet basic daily needs are not optimal (Karim et al., 2012).

9. The effect of BCG immunization on the incidence of clinical TB in children

The results of the study showed that children who received BCG immunization had a lower risk of developing TB by 0.12 times compared to children who did not receive BCG immunization. The results of the study showed that there was no significant effect between BCG immunization and TB status in children. This is not in line with research that states that children who do not receive age-appropriate BCG vaccination based on recommendations from the Indonesian Ministry of Health have a higher risk of developing TB than children who receive BCG vaccination (Hu et al., 2013). Jain et al., (2013) stated that the prevalence of TB in school children can be reduced by strengthening BCG vaccination in the national immunization program as an active TB prevention strategy (Setiyaningsih et al., 2019). Syahputra et al (2019) stated that the risk of TB increases if people never received BCG immunization (OR= 8.86; 95% CI= 3.28 to 23.94; p<0.001),

Judging from the BCG immunization perspective, toddlers who are not immunezed have a 4 times higher risk of contracting TB compared to those who are immunized with BCG. In household contact with TB patients (Jahiroh and Prihartono, 2013). According to Michelsen et al. (2014), the difference in results regarding the effecttiveness of BCG immunization is because giving the BCG vaccine does not mean preventing all primary TB infections but preventing more serious TB complications such as miliary TB and TB meningitis, so children can still be infected with TB.

10. The contextual influence of the village (village economic status) on the incidence of clinical TB in children

The results of the multilevel analysis show an ICC value = 52.95%, this indicator shows that the conditions of each village area have a contextual influence on variations in the incidence of TB in children. The epidemiological triangle theory explains that the emergence of a disease is caused by the influence of host, agent and environmental factors. The environment outside the individual (host) plays an important role in the increase in TB in children (Murti, 2016).

Poverty conditions affect the health behavior of the community in each village/ district which is also different (Bai et al., 2018). Villages with the majority of people have access to health information tend to have high awareness of health and will usually influence local residents to share their concern 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 less awareness of health, the surroundings environment can be affected, and do not care about negative behavior. (Cross et al., 2014).

The conclusion of this study is that the risk of clinical TB in children increases with stunting, a history of TB contact, exposure to cigarette smoke, decreases with healthy home sanitation, female gender, parental education ≥ and high school, there is no relationship between age, parental income, and BCG immunization status. This multilevel analysis shows the important role of contextual factors at the village level in influencing the incidence of clinical TB in children. The limitation of this study is that this study was only conducted in 82 villages in Wonogiri Regency, therefore, the results may not be directly applicable to child populations in other areas. In addition, this study used an analytical observational design with a case-control study approach, which may limit the ability to draw direct causal conclusions.

AUTHOR CONTRIBUTION

Khairina Nur Hidayati is the main researcher who developed the conceptual framework, collected data, analyzed the data and wrote the manuscript. Bhisma Murti helped to develop the conceptual framework, guided data analysis and interpreted the results of data analysis. Setyo Sri Rahardjo guided contextually in the discussion.

ACKNOWLEDGMENT

The author would like to thank the Head of the Health Service, Head of the Community Health Center, Village Head in Wonogiri Regency, Central Java who gave permission and helped with the data collection process. Thank you to all parties involved in collecting data for this study.

FUNDING AND SPONSORSHIP

This study is self-funded.

CONFLICT OF INTEREST

There is no conflict of interest in this study.

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