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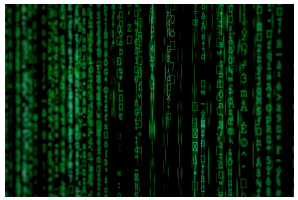

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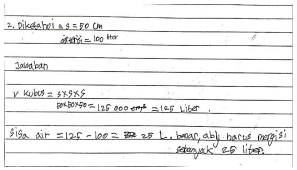

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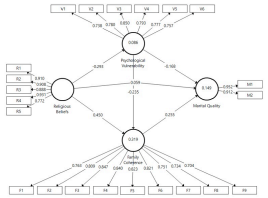

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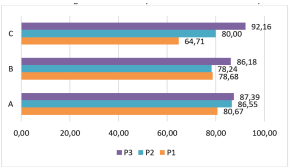

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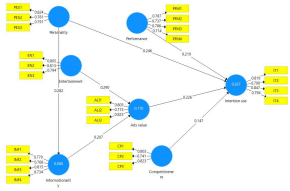

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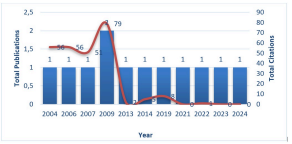

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Determining factors of lung tuberculosis among children in community health centers: A cross-sectional study

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Abstract Tuberculosis is a serious global health issue and is particularly prevalent among children. Early and correct diagnosis is very important for effective management, but tuberculosis diagnosis in children is often difficult because the clinical symptoms are nonspecific and difficult to collect specimens. This study aims to determine risk factors based on sociodemographic, socioeconomic, nutrition and clinical status associated with tuberculosis. This study is a cross-sectional study. Children aged 0 to 14 years who came to the community health center with one or more clinical symptoms related to TB from January to December 2023 were studied. Research participants underwent two diagnostic methods, clinical and bacteriological. Positive Clinical diagnosis was found to be 72.4%. Meanwhile, bacteriologically confirmed participants were 10.3%, the remainder were unable to produce sputum. Most respondents were men (62.8%), with 66% of respondents aged ≥5 years, and those sociodemographic factors have a significant relationship with tuberculosis in children ($p<0.05$). This study found that 64.7% of respondents had a BMI <18.5 and significantly related to tuberculosis in children ($p<0.05$). Furthermore, tuberculosis incidence and malnutrition also have a significant relationship ($p<0.05$). Contact with active tuberculosis cases shows a significant difference in the proportion of tuberculosis and nontuberculosis cases ($p=0.009$), while 57.1% of children were exposed to cigarette smoke ($p<0.05$). Government health insurance (BPJS) was used by 70.5% of respondents who were tested positive for tuberculosis, and it is statistically significant ($p<0.05$). Other socioeconomic factors were also significant ($p <0.05$) for tuberculosis cases in children whose parents had low education at 85.9%; have 96.8% of jobs with a household income equal to or more than the provincial minimum wage (UMP) of 60.3%. In the future, these factors can be utilized to construct prediction models for clinical diagnosis in children suspected of tuberculosis, especially machine learning-based models, in addition to tuberculosis-related clinical symptoms.

Keywords: pediatrics, exposure to tuberculosis, tuberculosis, risk factor

1. Introduction

Among the leading sources of morbidity and death in children aged 0–14 years are tuberculosis (TB), which accounts for approximately 12% of the total 10.6 million TB cases in the world in 2023 and contributes to 3–25% of the total TB cases (World Health Organization, 2023). Children might represent up to 20% of the global burden of TB at endemic locations; hence, the real situation can vary from forecasts given adequate reporting systems and appropriate diagnoses (Richens et al., 2020). Nevertheless, there is a fairly modest rate of TB-identified cases and notifications, particularly in developing nations with limited resources, such as Indonesia; the estimated TB incidence of children aged 0–14 in 2022 is 110,881 children, or approximately 15.3% of all TB cases in Indonesia (Ministry of Health of the Republic of Indonesia, 2023). According to a survey by the United Nations International Children's Emergency Fund (UNICEF), 35% of instances of TB among children between the ages of 0 and 14 are unreported, meaning that these 110,881 children constitute only 65% of the total child TB cases in 2022 (UNICEF Indonesia, 2022). These data indicate that the level of community transmission is relatively high.

Bacteriological testing is the standard diagnostic method for adult TB but has low sensitivity and specificity when used in children (Basile et al., 2022). Since the prevalence of TB in children serves as an immediate indicator and surrogate for TB spread in the community, there is a dearth of novel, easily used, and inexpensive diagnostic methods for TB, especially in remote areas with limited laboratory and X-ray facilities, which adds to existing problems (UNICEF Indonesia, 2022). The diagnosis of tuberculosis in children aged 0–14 years without specific symptoms is a major challenge for doctors, academics, and program managers because it can hinder diagnosis and lead to worse treatment outcomes (Siddalingaiah et al., 2023). Current diagnostic methods have limited sensitivity, especially in children aged 0–14 years (Namuganga et al., 2021). The

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scoring system, an alternative for diagnosing TB in children, has not yet been fully implemented according to guidelines (Ministry of Health of the Republic of Indonesia, 2023; World Health Organization, 2022).

In addition to clinical and biological variables, several socioeconomic and environmental variables increase the likelihood of TB in children between the ages of 0 and 14. These risk factors are very useful for predicting the development of TB disease. Therefore, identifying the risk factors for TB in children is crucial for making a diagnosis and initiating treatment as soon as possible for the best outcomes. Community health centers in Indonesia are the main place where TB patients seek treatment, so they are the starting point for TB case care, which includes early diagnosis, treatment, and reporting. The purpose of this study was to assess the sociodemographic, socioeconomic, and clinical risk factors for TB in children aged 0 to 14 years who exhibited one or more TB-related clinical symptoms.

2. Materials and methods

2.1. Data collection

This research was conducted at a community health center in the administrative area of South Jakarta, Indonesia. The respondents were children aged 0--14 years who came with a cough to receive treatment at community health centers between January and December 2023.

2.2. Research design

We used a cross-sectional design and studied children with normal nutritional status or malnutrition, including all genders, aged 0--14 years, who presented with a cough to receive treatment at community health centers between January and December 2023. The number of respondents was determined via consecutive sampling, and the sample size was determined via the total sampling method. All respondents who met the inclusion criteria were included in the study. TB diagnosis is categorized on the basis of clinical diagnosis (accompanied by X-rays and/or tuberculin tests) and bacteriology. The clinical diagnosis was determined by the occurrence or absence of symptoms of a persistent cough lasting more than 2 weeks, weight depletion or no weight gain in the previous two months, fever ≥2 weeks, and malaise ≥2 weeks. Sociodemographic factors (age, sex, age group, weight, height, nutritional status) were recorded during the medical history. Contact with active TB cases, history of BCG immunization, and exposure to cigarette smoke/air pollution were categorized dichotomously. Socioeconomic factors (education, employment, parental income, and health insurance) were also categorized dichotomously. This study also recorded the presence or absence of comorbid factors (HIV and DM). A child's nutritional status is determined by body mass index (BMI), which is calculated as the ratio of body weight in kilograms to height in meters squared. Furthermore, the BMI value of children aged 0–60 months must be compared with the WHO 2005 standard BMI value (WHO, 2006) and BMI values for children and adolescents (5–19 years old) in comparison to the WHO/NCHS 2007 reference (WHO, 2007).

2.3. Data analysis

All the data that had been collected and entered into standard Microsoft Excel were then analyzed via SPSS for Windows (SPSS Inc. version 25.0, Chicago, IL). The variables were initially examined univariately, and then a chi-square statistic was used to evaluate categorical variables to determine risk factors in children with tuberculosis. The McNemar statistic was used to estimate the proportions of risk variables between TB patients and non-TB patients. A statistically significant probability is smaller than 0.05. The odds ratio (OR) and 95% confidence interval (CI) were computed to ascertain the strength of the link.

3. Results and Discussion

The purpose of this cross-sectional study was to identify the predictive variables for both TB and non-TB diagnoses among children aged 0–14 years in Community Health Center facilities in Indonesia. TB risk factors such as HIV and diabetes were not found in the child respondents, so no analysis was carried out.

In this study, 113 out of 156 respondents were diagnosed with pulmonary TB from January to December 2023. Among the TB patients who received treatment, 72.4% of the respondents were clinically diagnosed with pulmonary TB. Bacteriologically confirmed TB cases were found in 10.3% of the respondents, and 89.7% of the respondents were unable to produce phlegm. Most of the respondents (62.8%) were boys, with 34% being less than five years old and 66% being older than five years (Table 1). Negative smear test results reportedly contribute to 13–20% of transmission and are, on average, 20–25% more infectious than positive test results (Asadi et al., 2022). Previous studies reported that most TB cases were diagnosed on the basis of clinical criteria (50–58%) (Chilyabanyama et al., 2024; Zürcher et al., 2019). Similarly, a previous cohort study reported that 16% (58/372), 95% CI, and 12–19% of the cases were smear-negative (Chilyabanyama et al., 2024), indicating that 84% of the TB cases were smear positive. However, another study reported that 65.2% of TB patients had negative BTA results and that 34.8% had positive BTA results (Campos et al., 2016).

Table 1 Characteristics related to sociodemographic factors, TB contact, BCG immunization, nutritional status, and exposure to smoking/air pollution between TB and non-TB respondents.

Characteristics	Frequency		TB	Non-TB	p Value	Odd Ratio (OR)	95% CI
	N, mean	%, SD					
Bacteriological diagnosis							
Yes	16	10.3	16	0	0.009*	-	-
No	140	89.7	97	43			
Age (year)							
<5 years	53	34	38	15	0.000¶	0.964	0.594 – 1.564
≥5 years	103	66	75	28		1.019	0.790 – 1.315
Gender							
Boy	98	62.8	72	26	0.000¶	1.054	0.797 – 1.393
Girl	58	37.2	41	17		0.918	0.589 – 1.429
Weight (kg)	19.6218	8.94918			0.000*	-	18.21 – 21.04
Height (cm)	104.3910	26.23235			0.000*	-	100.24 – 108.54
Body Mass Index (BMI)							
<18.5	101	64.7	91	10	0.000*	3.463	1.997 – 6.005
>18.4	55	35.3	22	33		0.254	0.168 – 0.382
Contacts with active TB patients							
Yes	85	54.5	62	23	0.002¶	1.026	0.741 – 1.420
None	71	45.5	51	20		0.970	0.664 – 1.418
BCG immunization							
Yes	114	73.1	85	29	0.328*	1.115	0.883 – 1.408
No	42	26.9	28	14		0.761	0.445 – 1.302
nutritional status							
Malnutrition	100	64.1	90	10	0.000*	3.425	1.974 – 5.941
Normal	56	35.9	23	33		0.265	0.178 – 0.396
Smoke exposure/air polution							
Yes	89	57.1	65	24	0.006¶	1.031	0.756 – 1.405
None	67	42.9	48	19		0.961	0.645 – 1.432

*Chi-square test, p value <0.05; ¶McNemar test, p value <0.05.

TB disease is generally determined on the basis of clinical diagnosis and is accepted when bacteriological evidence is unavailable (Abdullahi et al., 2021). As is often reported, most respondents were boys. Various studies have reported similar findings, with TB cases occurring more often in boys (Alao et al., 2020; Campos et al., 2016; Chidambaram et al., 2021) and variations in the age range of children who contract TB. Younger children are believed to be more affected than older children are (Hamid et al., 2019; Ogbudebe et al., 2018; Tilahun & Gebre-Selassie, 2016; Vukugah et al., 2022) due to household contact with active TB patients and immature immunity. However, exposure to active TB can also occur in the community. Boys tend toward physical activity and high socialization, so they enjoy playing outside the house. This causes boys to potentially encounter adult active TB and be exposed to cigarette smoke or air pollution (Martínez-Andrés et al., 2017; Miller et al., 2021).

Malnutrition and tuberculosis (TB) are reciprocally associated: malnutrition increases the likelihood of having active TB by six to ten times, and TB contributes to malnutrition in patients (Feleke et al., 2019; Musuenge et al., 2020). Patients with active TB tend to be underweight and have a BMI less than 18.5 kg/m2, which is considered an index of malnutrition. Thus, TB incidence is strongly correlated with poor nutrition and low BMI (Musuenge et al., 2020). The possibility of TB increases due to malnutrition, both micro- and macrodeficits, and compromised immunity. Infection with TB can intensify metabolism and require more energy, which can lead to eased appetite and nutritional malabsorption, ultimately increasing the possibility of being underweight (Feleke et al., 2019; Vonasek et al., 2022). A previous study revealed that, compared with the control group, TB patients had a greater likelihood of having a BMI of less than 18.5 kg/m2 (Kitonsa et al., 2020). The nutritional status in this study was assessed via BMI; 64.7% of the respondents had a BMI <18.5, which was significantly associated with the incidence of childhood TB ($p<0.05$).

This study revealed that 54.5% of the respondents had a history of interaction with active TB patients. The proportions of TB and non-TB cases in the child group differed significantly when the children were exposed to cases of active TB (p value=0.002). The strong connection between TB disease in children and a history of interaction with the source of TB cases is crucial since it is well known that the risk of developing TB is directly proportional to the number of germs to which a child is exposed (Koura et al., 2023). Multivariate analysis in previous research revealed a significant relationship between household contacts of children with active TB, with OR = 15 288 and 95% CI: 5,378–43 457; household contacts with smokers, with OR = 7,094 and 95% CI: 2,128–23 648; and contacts > 18 hours with TB sufferers, with OR = 4.681 and 95% CI: 1.198–18.294 (Laghari et al., 2019). Children under the age of five, especially those under 1 year, who meet a source of TB cases usually have a 50% chance of contracting TB, and ninety-five percent of TB cases occur within a year after contact. Home contacts, caregivers, and

medical professionals are considered close contacts of active tuberculosis patients (Patra et al., 2015) because they have a greater chance of contracting *Mycobacterium tuberculosis* and developing primary active tuberculosis (Rea et al., 2022; Reichler et al., 2018).

This study revealed that 73.1% of the respondents had been vaccinated against BCG. The sole licensed and amply used vaccine to prevent TB prompted by *M. tuberculosis* is Bacillus Calmette-Guérin (BCG) (Casey et al., 2016; Katelaris et al., 2019). BCG immunization is highly effective in preventing meningitis and miliary TB in children, with a 70 to 80% success rate (Katelaris et al., 2019; Roy et al., 2019). An 18-year cohort study in Tunisia reported that 36.5% of TB cases occurred in individuals who received BCG vaccination, whereas 63.3% of unvaccinated individuals did (Bennasrallah et al., 2019).

The respondents in this study more often had a history of exposure to cigarette smoke (57.1%), but none of the respondents had a history of HIV or diabetes (Table 1). In numerous countries where the prevalence of tuberculosis is high, most children are exposed to cigarette smoke or secondhand smoke. A comprehensive analysis encompassing eighteen observational studies revealed that exposure to tobacco-related smoke resulted in children being 3.41 times more likely to contract tuberculosis and 1.64 times more likely to develop latent tuberculosis infection (Patra et al., 2015). Research in Spain reported that exposure to cigarette smoke in children (95% CI: 9.63–18.17) increased the prevalence of TB (13.48%) (Altet et al., 2022). Greater vulnerability to pulmonary tuberculosis has been attributed to several biological factors, including poor mucosal secretion clearance, impaired alveolar macrophage phagocytic capacity, diminished immunological reactions, and/or CD4+ lymphopenia caused by cigarette nicotine (Burusie, Enquesilassie, Addissie, Dessalegn, & Lamaro, 2020; Wang et al., 2020). Another study that examined the relationship between TB disease and exposure to cigarette smoke reported that the detrimental impact of smoking on tuberculosis transmission was significantly reduced immediately after smoking cessation, highlighting the value of smoking cessation programs in the fight against TB (Chu et al., 2021). Case–control studies carried out in Brazil and India have shown that firewood or biomass smoke, apart from cigarette smoke, is a separate threat to TB. However, there is currently still a dearth of information about the pathway through which biomass smoke results in chronic pulmonary illness (Báez-Saldaña et al., 2021; Sarkar et al., 2017).

The World Health Organization (WHO) lists fever, inexplicable weight decrease, lethargy or exhaustion, sweating at night, chest pain, and cough lasting longer than two weeks as manifestations and indicators of TB (World Health Organization, 2024). Given the risk of overdue diagnosis in those infected and subsequent spread via close contacts, over time, cough is the most noticed manifestation of tuberculosis, thus summoning inquiry, particularly in resource-constrained states where tuberculosis incidence rises (defined as ≥100 in 100 000 inhabitants) (Field et al., 2018). Most respondents in the current study, 79.5%, came to the health center with cough symptoms, and the remaining 20.5% did not experience cough complaints. The change in body weight was not very different; only 49.4% of the respondents experienced weight loss. A total of 55.8% of the respondents had a fever, and 44.2% did not have a fever; malaise was present in 59.6% of the respondents, and 40.4% did not have malaise (Table 1). In the study population conducted in the Philippines, which provided positive TB test results, 84.9% of patients experienced cough ≥ 2 weeks, fever ≥ 2 weeks of unexplained cause (6.9%), and considerable and unintended weight loss (9.5%), and 6.3% of patients experienced exhaustion, sluggishness, and malaise (Lee et al., 2019). The findings of these studies revealed that all participants with cough symptoms, regardless of the length of time for TB examination, presented increased sensitivity from forty-two percent to fifty-one percent (Cheng et al., 2015).

This research revealed that 70.5% of respondents who had national health insurance facilities (BPJS) and 75.5% of respondents tested positive for pulmonary TB. Meanwhile, research in the Philippines reported that 16% of individuals who tested positive for TB were enrolled in a health insurance program (51%) (Lee et al., 2019). Since TB is known to be a disease of poverty, the national health insurance program in Indonesia both improves the capacity of TB patients to seek treatment and contributes significantly to the TB reporting rate. Another study revealed that 60.3% of patients' household income was either per or exceeded the provincial minimum wage (UMP). Almost all the respondents' parents had jobs, 96.8% of

Whom were grouped as nongovernment workers (85.1%) or government workers (10.9%), but only 14.1% had higher education (Table 2). A systematic review revealed a correlation between tuberculosis and poor educational attainment, with a pooled odds ratio of 2.34 (Ricvan Dana et al., 2024). In a South African study including adolescents aged 12 to 18 years, the characteristics that were predictive of TB were older age, ethnic background, low household earnings, and basic schooling or less for both parents (Tchakounte et al., 2022).

With respect to socioeconomic factors (Table 2), TB in childhood occurs more often in families with lower parental education ($p = 0.005$), parents who have jobs ($p < 0.001$), parents with incomes greater than or equal to the UMP ($p < 0.001$), and those with health insurance ($p < 0.001$). The associations between clinical features and the incidence of bacteriological TB in pediatric patients are displayed in Table 3. Symptoms of cough ($p < 0.001$), subfebrile fever ($p < 0.001$), malaise ($p < 0.001$), and weight loss or no weight gain ($p < 0.001$) were significantly different between TB and non-TB events. Owing to the correlation with the increasing prevalence of TB, socioeconomic determinants are linked to the availability of healthcare services, the capacity to fulfill nutritional demands, and the availability of decent and standardized living spaces (Hameed e al., 2019). Working parents are linked to the external environment and to tuberculosis infection, which can spread to children. The exposure that children obtain from a household member who has TB is nearly fourfold inclined to contract the disease (Long et al., 2022; Martinez et al., 2017).

Table 2 Characteristics related to socioeconomic factors, clinical symptoms, and smoke exposure between TB and non-TB respondents.

Characteristics	Frequency		TB	Non-TB	p Value*	Odd Ratio (OR)	95% CI
	N, mean	%, SD					
Parents education							
Low	134	85.9	97	37	0.005¶	0.998	0.66 – 1.150
High	22	14.1	16	6		1.015	0.425 – 2.422
Parents occupation							
Not working	5	3.2	4	1	0.000¶	1.522	0.175 – 13.238
Working	151	96.8	109	42		0.988	0.932 – 1.047
Household income							
< UMP	62	39.7	42	20	0.000¶	0.799	0.536 – 1.192
>= UMP	94	60.3	71	23		1.175	0.859 – 1.606
Government health insurance							
None	46	29.5	30	16	0.000¶	0.713	0.435 – 1.170
Yes	110	70.5	83	27		1.170	0.906 – 1.510
Chronic coughing ≥2 weeks							
Yes	124	79.5	90	34	0.937*	1.007	0.842 – 1.206
None	32	20.5	23	9		0.972	0.490 – 1.931
Weight loss or does not increase in the last 2 months							
Yes	77	49.4	60	17	0.000¶	1.343	0.893 – 2.020
None	79	50.6	53	26		0.776	0.568 – 1.059
Subfebris febris ≥2 weeks							
Yes	87	55.8	63	24	0.003¶	0.999	0.731 – 1.365
None	69	44.2	50	19		1.001	0.675 – 1.486
Malaise ≥ 2 weeks							
Yes	93	59.6	67	26	0.024¶	0.981	0.737 – 1.305
None	63	40.4	46	17		1.030	0.669 – 1.585

*Chi-square test, p value <0.05; ¶*McNemar test, p value <0.05*. UMP = provincial minimum wage.

Table 3 Characteristics related to clinical factors among TB and non-TB respondents on the basis of bacteriological diagnosis.

Characteristics	Frequency		TB	Non-TB	p Value*	Odd Ratio (OR)	95% CI
	N, mean	%, SD					
Chronic cough ≥2 weeks							
Yes	124	79.5	14	110	0.000¶	1.114	0.908 – 1.366
2. None	32	20.5	2	30		0.583	0.154 – 2.216
Weight drop or did not rise in the previous 2 months							
Yes	77	49.4	7	70	0.000¶	0.875	0.490 – 1.562
2. None	79	50.6	9	70		1.125	0.708 – 1.787
Subfebris fever ≥2 weeks							
Yes	87	55.8	11	76	0.000¶	1.266	0.880 – 1.822
2. None	69	44.2	5	64		0.684	0.323 – 1.446
Malaise ≥ 2 weeks							
Yes	93	59.6	10	83	0.000¶	1.054	0.704 – 1.578
2. None	63	40.4	6	57		0.921	0.474 – 1.788

¶McNemar test, p value <0.05.

4. Conclusions

Despite this modest study, this study underscores the importance of sociodemographic factors, socioeconomic factors, active TB contacts, malnutrition conditions, and exposure to cigarette smoke or air pollution in the diagnosis of TB in children, in addition to TB-related clinical symptoms (cough, fever, malaise, and weight loss).

Ethical considerations

All procedures involving patients in this study were approved by the Ethical Review Committee of the Faculty of Medicine, Trisakti University No.055/KER/FK/I/2024. Informed consent was signed by all patients' legal guardians.

Conflict of interest

The authors have disclosed no conflicts of interest.

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Determining Factors of Lung Tuberculosis among Indonesian Children in Community Health Centers: A Cross-sectional Study

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Abstract

Background: Tuberculosis is a serious global health issue and is particularly prevalent among children. Early and correct diagnosis is very important for effective management, but tuberculosis diagnosis in children is often difficult because the clinical symptoms are non-specific and difficult to collect specimens. This study aims to determine risk factors based on sociodemographic, socioeconomic, nutrition and clinical status associated with tuberculosis. **Methods:** This study is a cross-sectional study. Children aged 0 to 14 years who came to the community health center with one or more clinical symptoms related to TB from January to December 2023 were studied. Research participants underwent two diagnostic methods, clinical and bacteriological. **Results:** Positif Clinical diagnosis was found to be 72.4%. Meanwhile, bacteriologically confirmed participants were 10.3%, the remainder were unable to produce sputum. Most respondents were men (62.8%), with 66% of respondents aged ≥5 years, and those sociodemographic factors have a significant relationship with tuberculosis in children ($p<0.05$). This study found that 64.7% of respondents had a BMI <18.5 and significantly related to tuberculosis in children ($p<0.05$). Furthermore, tuberculosis incidence and malnutrition also have a significant relationship ($p<0.05$). Contact with active tuberculosis cases shows a significant difference in the proportion of tuberculosis and non-tuberculosis cases ($p=0.009$), while 57.1% of children were exposed to cigarette smoke ($p<0.05$). Government health insurance (BPJS) was used by 70.5% of respondents who were tested positive for tuberculosis, and it is statistically significant ($p<0.05$). Other socio-economic factors were also significant ($p <0.05$) for tuberculosis cases in children whose parents had low education at 85.9%; have 96.8% of jobs with a household income equal to or more than the provincial minimum wage (UMP) of 60.3%. **Conclusion:** In the future, these factors can be utilized to construct prediction models for clinical diagnosis in children suspected of tuberculosis, especially machine learning-based models, in addition to tuberculosis-related clinical symptoms.

Keyword: pediatrics, contact with active tuberculosis cases, tuberculosis, risk factor, comorbidity

Introduction

Among the leading source for morbidity and death in children aged 0 – 14 years is tuberculosis (TB), which is around 12% of the total 10.6 million TB sufferers in the world in 2023 and contributes to 3 – 25% of the total TB caseload [1]. Children might represent up to 20% of the global burden of TB in endemic spots, hence the real situation can vary from forecasts given

adequate reporting systems and appropriate diagnosis [2]. Still, there is a fairly modest rate of TB identified cases and notification, particularly in developing nations with limited resources, such as Indonesia, the estimated TB incidence of children aged 0 – 14 in 2022 is 110,881 children or around 15.3% of all TB cases in Indonesia [3]. According to a survey by The United Nations International Children's Emergency Fund (UNICEF), 35 percent of instances of TB among children between the ages of 0 and 14 go unreported, meaning these 110,881 children are only 65% of the total child TB cases in 2022 [4]. Mentioned data indicate the level of community transmission is relatively high.

Bacteriological testing is the standard diagnosis in adult TB but has low sensitivity and specificity when used in children [5]. Since the prevalence of TB in children serves as an immediate clue and surrogate for TB spreads in the community, there is a dearth of novel, easily used, and inexpensive diagnostic methods for TB, especially in remote areas with limited laboratory and x-ray facilities, adds to existing problems [4]. Diagnosis of tuberculosis in children aged 0 – 14 years without specific symptoms is a big challenge for doctors, academics, and program managers because it can hinder diagnosis and lead to worse treatment outcomes [6]. Current diagnostic methods have limited sensitivity, especially in children aged 0 – 14 years [7]. The scoring system, which is an alternative for diagnosing TB in children, is not yet fully implemented according to guidelines [3,8].

Despite clinical and biological variables, there are several socioeconomic and environmental variables that increase the likelihood of TB in children between the ages of 0 and 14. These risk factors are very useful for predicting the development of TB disease. Therefore, knowing the risk factors for TB in children is crucial for making the diagnosis and initiating treatment as soon as possible for the best outcomes. Community health centers in Indonesia are the main place where TB patients seek treatment, so they are the starting point for TB case care which includes early diagnosis, treatment, and reporting. The purpose of this study is to assess the sociodemographic, socioeconomic, and clinical risk factors for TB in children ages 0 to 14 who exhibit one or more TB-related clinical symptoms.

Material and Methods

Data collection

This research was conducted at a community health center in the administrative area of South Jakarta, Indonesia. The respondents are children, aged 0 to 14 years, who came with a cough to receive treatment at the community health centers, between January and December 2023.

Research design

We used a cross-sectional design and studied children with normal nutritional status or malnutrition, including all genders, aged 0 to 14 years, who came with a cough to receive treatment at the community health centers, between January and December 2023. Respondents were determined using consecutive sampling and the sample size was determined using the total sampling method, all respondents who met the inclusion criteria would be included in the study.TB diagnosis is categorized based on clinical diagnosis (accompanied by x-rays and/or tuberculin tests) and bacteriology. The clinical diagnosis was determined by the occurrence or absence of symptoms of a persistent cough lasting more than 2 weeks, weight depletion or no weight gain in the previous two months, fever ≥2 weeks, and malaise ≥2 weeks. Socio-demographic factors (age, gender, age group, weight, height, nutritional status) were recorded during the history taking.

Contact with active TB cases, history of BCG immunization and exposure to cigarette smoke/air pollution were categorized dichotomously. Socio-economic factors (education, employment and parental income, and health insurance) were also categorized dichotomously. This study also recorded the presence or absence of comorbid factors (HIV and DM). A child's nutritional status is determined by the body mass index, or BMI, is calculated using the ratio between body weight in kilograms and height in meters squared. Furthermore, the BMI value of children aged 0-60 months must be compared with the WHO 2005 standard BMI value (WHO, 2006); and BMI values for children and adolescents (5–19 years old) in comparison to the WHO/NCHS 2007 reference (WHO, 2007).

Data analysis

All data that had been collected and entered standard Microsoft Excel was then analyzed using SPSS for Windows (SPSS Inc version 25.0, Chicago, IL). Variables were initially examined univariately, and then a Chi-square statistic was used to evaluate categorical variables in order to determine risk factors in children with tuberculosis. The McNemar statistic was used to estimate the proportion of risk variables between TB and non-TB patients. A statistically significant probability if smaller than 0.05. The odds ratio (OR) and 95% confidence interval (CI) were computed to ascertain the strength of the link.

Results

In this study, 113 out of 156 respondents were diagnosed with pulmonary TB from January to December 2023. Of the TB cases who received treatment, 72.4% of respondents were clinically diagnosed with pulmonary TB. Meanwhile, bacteriologically confirmed TB cases were found in 10.3% of respondents and 89.7% of respondents were unable to produce phlegm. Most of responders (62.8%) were boys, with 34% being less than five years old and 66% being older than five (**Table 1**).

The nutritional status was assessed using the BMI, 64.7% of respondents had a BMI <18.5 and it was significantly associated with the incidence of childhood TB ($p<0.05$). A previous record of interaction with active tuberculosis patients was reported by 54.5% of the respondents. The proportion of TB and non-TB occurrences in the child group differs significantly when exposed to cases of active TB (p-value=0.002). Most respondents received BCG immunization, namely 73.1%. Respondents more often had a history of exposure to cigarette smoke, namely 57.1%, but all respondents did not have a history of HIV and diabetes (**Table 1**).

Most respondents came to the health center with cough symptoms, namely 79.5% and the remaining 20.5% did not experience cough complaints. The change in body weight was not much different, only 49.4% of respondents experienced weight loss. 55.8% of respondents had fever and 44.2% did not have fever, malaise was present in 59.6% of respondents and 40.4% did not have malaise (**Table 1**). All respondents did not use private insurance, but most respondents used BPJS insurance facilities, 70.5%, while 29.5% did not have insurance. Most of the patient's household income corresponds to or exceeds the provincial minimum wage (UMP) of 60.3%. Almost all the respondents' parents had jobs, 96.8% of whom were grouped as non-PNS 85.9% and PNS 10.9%, but only 14.1% had higher education (**Table 2**).

Most respondents were diagnosed with TB based on clinical diagnosis, because it was difficult to obtain children's sputum specimens for bacteriological examination. A bacteriological diagnosis could only be made in 10.3% of respondents and the majority (81.25%) were >10 years old. According to sociodemographic data (**Table 1**) indicates that there are statistically significant

variations in proportions of boys and girls ($p<0.001$), body weight ($p<0.001$), height ($p<0.001$). This study showed a notable association between the incidence of TB and nutritional status ($p=0.035$), exposure to cigarette smoke or air pollution ($p=0.006$), but not significantly with BCG immunization ($p=0.328$).

Regarding socioeconomic factors (**Table 2**), TB in childhood occurs more often in families with lower parental education ($p=0.005$), parents who have jobs ($p<0.001$), parental income greater than or equal to the UMP ($p<0.001$) and have health insurance ($p<0.001$). The association among clinical features and the incidence of pediatric TB patients with bacteriological diagnosis is displayed in **Table 3**. Symptoms of cough ($p<0.001$), subfebrile fever ($p<0.001$), malaise ($p<0.001$), and weight loss or no weight gain ($p<0.001$) showed significant differences in proportion between TB and non-TB events.

Table 1. Characteristics related to sociodemographic factors, TB contact, BCG immunization, nutritional status, and Exposure to smoking/air pollution between TB and non-TB respondents.

Characteristics	Frequency		TB	Non-TB	p-Value	Odd Ratio (OR)	95% CI
	N, mean	%, SD					
Bacteriological diagnosis							
1.Yes 2.No	16 140	10.3 89.7	16 97	0 43	**0.009***	-	-
Age (year)							
1.<5 years **2.**≥5 years	53 103	34 66	38 75	15 28	**0.000¶**	0.964 1.019	0.594 – 1.564 0.790 – 1.315
Gender							
1.Boy 2.Girl	98 58	62.8 37.2	72 41	26 17	**0.000¶**	1.054 0.918	0.797 – 1.393 0.589 – 1.429
Weight (kg)	19.6218	8.94918			**0.000***	-	18.21 – 21.04
Height (cm)	104.3910	26.23235			**0.000***	-	100.24 – 108.54
Body Mass Index (BMI)							
1.<18.5 **2.**>18.4	101 55	64.7 35.3	91 22	10 33	**0.000***	3.463 0.254	1.997 – 6.005 0.168 – 0.382
Contacts with active TB patients							
1.Yes 2.None	85 71	54.5 45.5	62 51	23 20	**0.002¶**	1.026 0.970	0.741 – 1.420 0.664 – 1.418
BCG immunization							
1.Yes 2.No	114 42	73.1 26.9	85 28	29 14	0.328*	1.115 0.761	0.883 – 1.408 0.445 – 1.302
nutritional status							
1.Malnutrition 2.Normal	100 56	64.1 35.9	90 23	10 33	**0.000***	3.425 0.265	1.974 – 5.941 0.178 – 0.396

Smoke exposure/air polution							
1.Yes	89	57.1	65	24	**0.006¶**	1.031	0.756 – 1.405
2.None	67	42.9	48	19		0.961	0.645 – 1.432

**Chi-square test, p-value <0.05; ¶McNemar test, p-value <0.05*

Table 2. Characteristics related to socioeconomic factors, clinical symptoms, and smoke exposure between TB and non-TB respondents.

Characteristics	Frequency		TB	Non-TB	p-Value*	Odd Ratio (OR)	95% CI
	N, mean	%, SD					
Parents education							
1.Low **2.**High	134 22	85.9 14.1	97 16	37 6	**0.005¶**	0.998 1.015	0.66 – 1.150 0.425 – 2.422
Parents occupation							
• Not working • Working	5 151	3.2 96.8	4 109	1 42	**0.000¶**	1.522 0.988	0.175 – 13.238 0.932 – 1.047
Household income							
• < UMP • >= UMP	62 94	39.7 60.3	42 71	20 23	**0.000¶**	0.799 1.175	0.536 – 1.192 0.859 – 1.606
Government health insurance							
1. None 2. Yes	46 110	29.5 70.5	30 83	16 27	**0.000¶**	0.713 1.170	0.435 – 1.170 0.906 – 1.510
Chronic coughing ≥2 weeks							
1. Yes 2. None	124 32	79.5 20.5	90 23	34 9	0.937*	1.007 0.972	0.842 – 1.206 0.490 – 1.931
Weight loss or does not increase in the last 2 months							
1.Yes 2.None	77 79	49.4 50.6	60 53	17 26	**0.000¶**	1.343 0.776	0.893 – 2.020 0.568 – 1.059
Subfebris febris ≥2 weeks							
1.Yes 2.None	87 69	55.8 44.2	63 50	24 19	**0.003¶**	0.999 1.001	0.731 – 1.365 0.675 – 1.486

Malaise ≥ 2 weeks							
1.Yes 2.None	93 63	59.6 40.4	67 46	26 17	**0.024¶**	0.981 1.030	0.737 – 1.305 0.669 – 1.585

**Chi-square test, p-value <0.05; ¶McNemar test, p-value <0.05.*

Table 3. Characteristics related to clinical factors among TB and non-TB respondents based on bacteriological diagnosis

Characteristics	Frequency		TB	Non-TB	p-Value*	Odd Ratio (OR)	95% CI
	N, mean	%, SD					
Chronic cough ≥2 weeks							
1.Yes	124	79.5	14	110	**0.000¶**	1.114	0.908 – 1.366
2.None	32	20.5	2	30		0.583	0.154 – 2.216
weight drop or did not rise in the previous 2 months							
1.Yes	77	49.4	7	70	**0.000¶**	0.875	0.490 – 1.562
2.None	79	50.6	9	70		1.125	0.708 – 1.787
Subfebris fever ≥2 weeks							
1.Yes	87	55.8	11	76	**0.000¶**	1.266	0.880 – 1.822
2.None	69	44.2	5	64		0.684	0.323 – 1.446
Malaise ≥ 2 weeks							
1.Yes	93	59.6	10	83	**0.000¶**	1.054	0.704 – 1.578
2.None	63	40.4	6	57		0.921	0.474 – 1.788

¶*McNemar test, p-value <0.05*

Discussion

The purpose of this cross-sectional study was to identify the predictive variables for both TB and non-TB diagnoses among children aged 0 – 14 years in Community Health Center facilities in Indonesia. TB risk factors such as HIV and diabetes were not found in child respondents, so no analysis was carried out.

Participants in this study underwent two diagnostic methods, namely clinical and bacteriological. Negative smear test results reportedly contribute to 13–20% of transmission and are, on average, 20–25% more infectious than those with positive test results [9]. Previous studies reported that most TB cases were diagnosed based on clinical criteria (50 – 58%) [10,11]. Likewise, a previous cohort study found 16% (58/372), 95% CI, 12-19% of cases came from smear negative sources [9], meaning 84% of TB cases were smear positive. However, another study reported that 65.2% of TB patients had negative BTA results and 34.8% had positive BTA results [12]. In children, TB disease is generally determined based on clinical diagnosis, which is the accepted method when bacteriological evidence is not available [13]. As is often reported, most respondents were boys. Various studies have similar findings where TB cases occur more often in boys [12,14,15] and variations in the age range of children who contract TB. Younger children are believed to be more affected than older children [16-19] due to household contacts of active TB patients and immature immunity. However, exposure to active TB can also occur in the community. Boys have a tendency for physical activity and high socialization, so they enjoy playing outside the house. This causes boys to potentially encounter adult active TB and be exposed to cigarette smoke or air pollution [20,21].

Malnutrition and tuberculosis (TB) have a reciprocal association in which malnutrition raises the likelihood of getting active TB by six to ten times and TB contributes patients to malnutrition [22,23]. Patients with active TB tend to be underweight, having a BMI below 18.5 kg/m2, which is considered an index of malnutrition. Thus, TB incidence is strongly correlated with poor nutrition and lowly BMI [23]. The possibility of TB increases due to malnutrition, both micro and macro deficits, compromised immunity. Being infected with TB can intensify metabolism and require more energy, which can lead to ease appetites and nutrition malabsorption, ultimately raising the possibility of underweight [22,24]. Previous study found that, compared to the control group, TB patients had a higher likelihood of having a BMI of less than 18.5 kg/m2 [25]. Numerous countries where tuberculosis prevalence is elevated, most children are exposed to cigarette smoke or secondhand smoke. A comprehensive analysis encompassing eighteen observational studies revealed that exposure to tobacco-related smoke resulted in children being 3.41 times more likely to contract tuberculosis and a 1.64-times more likely to develop latent tuberculosis infection [26]. Research in Spain reported that exposure to cigarette smoke in children (95% CI: 9.63–18.17) and had an increased prevalence of TB (13.48%) [27]. Higher vulnerability to pulmonary tuberculosis illness has been attributed to several biological factors, including poor mucosal secretion clearance, impaired alveolar macrophage phagocytic capacity, diminished immunological reaction, and/or CD4+ lymphopenia brought on by cigarette nicotine [28,29]. Another study that looked at the relationship between TB disease and exposure to cigarette smoke also reported that the detrimental impact of smoking on tuberculosis transmission was significantly reduced immediately after smoking cessation, hence highlighting the value of smoking cessation programs in the fight against TB [30]. Case-control studies carried out in Brazil and India have shown that firewood or biomass smoke, apart from cigarette smoke, is a separate threat to TB. But there is currently still a dearth of information about the pathway via which biomass smoke results in chronic pulmonary illness [31,32].

Noticing a high connection between TB disease in children and a history of interaction with the source of TB cases is crucial since it is well-known that the risk of developing TB is directly

proportionate to the quantity of germs one receives exposure to [33]. Multivariate analysis in previous research showed a significant relationship between household contacts of children with active TB, obtained OR = 15,288 and 95% CI: 5,378–43,457, household contacts with smokers obtained OR = 7,094 and 95% CI: 2,128–23,648, contacts > 18 hours with TB sufferers obtained OR = 4.681 and 95% CI: 1.198–18.294 [34]. Children beneath the age of five, especially under 1 year, who meet a source of TB cases usually have a 50% chance of contracting TB, and ninety-five percent of TB occurs within a year after contact. Home contacts, caregivers, and medical professionals are considered close contacts of active tuberculosis cases [26] because they have a greater chance of contracting *Mycobacterium tuberculosis* and developing primary active tuberculosis [35,36].

The sole licensed and amply used vaccine to prevent TB prompted by *M. tuberculosis* is Bacillus Calmette-Guérin (BCG) [37,38]. The BCG immunization has been shown to be highly effective in preventing meningitis and miliary TB in children, with a 70 to 80 percent success rate [37, 39]. An 18-year cohort study in Tunisia found 36.5% of TB cases in individuals who received BCG vaccination compared to 63.3% of unvaccinated individuals [40]. The World Health Organization (WHO) lists fever, inexplicable weight decrease, lethargy or exhaustion, sweating at night, chest pain, and cough lasting longer than two weeks as manifestation and indicators of TB. Given the risk of overdue diagnosis in those infected and subsequent spread via close contacts, overtime cough is the most noticed manifestation in tuberculosis thus summons inquiry, particularly in resource-constrained states where tuberculosis incidence rises (defined as ≥100 in 100,000 inhabitants) [41]. In the study population conducted in the Philippines, providing positive TB test results, 84.9% experienced cough ≥ 2 weeks, fever ≥ 2 weeks of unexplained cause (6.9%), considerable and unintended weight loss (9.5%), and 6.3% of patients experienced exhaustion, sluggishness, and malaise [42]. Study finding concluded that all participants with cough symptoms of whichever length for TB examining versed rose sensitivity from forty-two percent to fifty-one percent [43].

This research shows that 70.5% of respondents who have national health insurance facilities (BPJS), 75.5% of respondents tested positive for pulmonary TB. Meanwhile, research in the Philippines reported that 16% of individuals who tested positive for TB were enrolled in a health insurance program (51%) [42]. Since TB is known to be a disease of poverty, national health insurance program in Indonesia's both improves the capacity of TB patients to seek treatment and contributes significantly to TB reporting rate. The study's finding revealed the respondents' parents who were positive for TB had non-PNS jobs with a household income equal to or more than the provincial minimum wage but had low education. A systematic review of studies found a correlation between tuberculosis and a poor educational attainment with a pooled odds ratio = 2.34 [44]. In a South African study including adolescents aged 12 to 18, characteristics that were predictive of TB were older age, ethnic background, low household earning, and basic schooling or lesser for both parents [45]. Due to the correlation with the increasing prevalence of TB, socioeconomic determinants are linked to the availability of healthcare services, the capacity to fulfill nutrition demands, also the availability of a decent and standardized living space [46]. Working parents are linked to external environment and tuberculosis infection, which can spread to children. Exposure that children obtain from a household member who has TB is nearly fourfold inclined to contract the disease [47,48].

Conclusion

Despite the modest study, this study underscores the importance of sociodemographic, socioeconomic, active TB contacts, malnutrition conditions, and exposure to cigarette smoke or air pollution in the diagnosis of tuberculosis in children, in addition to TB-related clinical symptoms (cough, fever, malaise, and weight loss).

Study limitations
This research was conducted at a community health center and there were no patient home visits so it did not analyze environmental factors which are one of the determinants of TB. However, other factors managed to show meaningful results.

Ethical considerations
All procedures involving patients in this study were approved by the Ethical Review Committee of the Faculty of Medicine, Trisakti University No.055/KER/FK/I/2024. Informed consent was signed by all patients' legal guardians.

Acknowledgments
Not Applicable.

Conflict of Interest
The authors have disclosed no conflicts of interest.

Availability of data and materials
The corresponding author will make the datasets used and/or analyzed in this work accessible upon an acceptable request.

Authors' contributions
M.M: study concept, writing up, data interpretation, methodology writing, statistical analysis, Finalize the manuscript revisions and provide approval.
A.B: study concept, revise manuscript, and provide final approval.
Y.Y: data collection, revise manuscript, and provide final approval.

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