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Drug-resistant tuberculosis in children in Indonesia: A population-based analysis of the 2023 Indonesian Health Survey

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ABSTRACT

Objective: To analyze the prevalence and risk factors of drug-resistant tuberculosis (DR-TB) among Indonesian children.

Methods: This study analyzed data from the 2023 Indonesian Health Survey, which included children aged 0-14 years and household heads nationwide. Binary logistic regression was used to identify factors associated with DR-TB.

Results: A total of 423 participants were included in the final analysis. The national prevalence of pediatric DR-TB was 15.9%, with substantial variation across provinces. In the multivariable logistic regression analysis, rural residence (a*OR* 2.68; 95% *CI* 1.23-5.84), poor TB treatment adherence (a*OR* 17.353; 95% *CI* 3.098-97.206), and household TB contact (a*OR* 5.628; 95% *CI* 1.113-28.450) were independently associated with higher odds of DR-TB. Wealth index was significantly associated with DR-TB overall (*P*=0.018), but no significant differences were observed between individual wealth categories after adjustment. Household TB contact was associated with higher odds of DR-TB (a*OR* 5.628; 95% *CI* 1.113-28.450).

Conclusions: Pediatric DR-TB in Indonesia has a substantial prevalence and marked geographic variation. Rural residence, poor TB treatment adherence, and household TB contact were key factors associated with DR-TB, highlighting the need to strengthen treatment adherence, household contact investigation, and targeted interventions.

KEYWORDS: Tuberculosis; Drug resistant tuberculosis; Child; Prevalence; Socioeconomic factors; Indonesia

1. Introduction

Tuberculosis (TB) remains a major global public health challenge, particularly in high-burden countries such as Indonesia. According to the World Health Organization (WHO), approximately 10.6

Summary

Question: What is the prevalence of drug-resistant tuberculosis (DR-TB) among Indonesian children, and what factors are associated with its occurrence?

Findings: In this cross-sectional analysis of 423 children from the 2023 Indonesian Health Survey, the national prevalence of DR-TB was 15.9%. Rural residence, poor TB treatment adherence, and household TB contact were associated with higher odds of DR-TB, while wealth index was significant overall.

Meaning: Strengthening treatment adherence, household contact management, and targeted interventions in rural areas may help reduce the burden of pediatric DR-TB in Indonesia.

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million people developed TB globally in 2023, including around 12% of children under 15 years of age[1]. Indonesia ranks second globally in terms of TB burden, with approximately 885 000 reported cases in 2024, including around 135 000 cases among children aged 0-14 years[2]. The emergence of drug-resistant tuberculosis (DR-TB), particularly multidrug-resistant/rifampicin-resistant TB (MDR/RR-TB), has further complicated TB control efforts due to prolonged treatment duration, increased toxicity, higher treatment costs, and poorer outcomes[3]. DR-TB refers to tuberculosis caused by *Mycobacterium* (*M.*) *tuberculosis* strains resistant to at least one anti-tuberculosis drug[4]. In pediatric populations, the burden of DR-TB is particularly concerning because diagnosis is often difficult due to nonspecific clinical manifestations, limited bacteriological confirmation, and restricted access to diagnostic and treatment services[5].

Globally, the prevalence of DR-TB is estimated at 11.6%, and the 2023 report by the World Health Organization highlighted an increase in pediatric TB cases, emphasizing the persistent high risk of drug resistance. In Indonesia, the incidence of DR-TB in 2022 was estimated at 10 cases per 100 000 population, equivalent to approximately 28 000 cases[1]. The number of TB drug-resistance examinations increased from 565 315 cases in 2020 to 2 317 381 cases in 2022, accompanied by an increase in notified DR-TB cases from 7 921 to 12 788 cases (50.8%). However, the proportion of patients initiating second-line treatment remained low at 58% in 2022[6]. Data on pediatric DR-TB in Indonesia remain limited, although cases among children aged <15 years increased from 4 cases in 2014 to 80 cases in 2021, with the number of patients initiating treatment increasing from 2 to 44[7,8]. National reports have shown an increase in DR-TB testing and case notifications in recent years; however, substantial gaps persist between diagnosis, treatment initiation, and treatment completion. The increasing burden of TB and drug resistance in Indonesia underscores the need to strengthen diagnostic services and national TB control programs[9].

DR-TB in children imposes considerable clinical and public health burdens. Treatment regimens are typically longer, more toxic, and associated with substantial adverse effects, while treatment outcomes remain variable[10]. Only approximately 3%-4% of pediatric DR-TB cases are microbiologically diagnosed and treated, while mortality, treatment failure, and loss to follow-up remain significant[11]. The treatment success rate of pediatric MDR-TB is approximately 77%, with mortality and loss to follow-up rates of 8% and 10%, respectively[12]. Its impact includes growth impairment and pulmonary disability, while low detection rates and limited access to second-line therapy further increase the risk of transmission and progressive drug resistance[13]. A cohort study conducted at Hasan Sadikin Hospital demonstrated that fewer than one-third of children and adolescents at risk for MDR-TB were successfully identified and tested, only 9.8% were diagnosed, 45.1% initiated treatment, and 25.5% completed therapy[14]. Accoridng to a systematic review, other studies have shown that HIV infection, malnutrition, and clinical TB characteristics significantly influence treatment outcomes in pediatric MDR-TB patients[14]. However, most existing studies in Indonesia have been conducted at health facility or referral-center levels and therefore may not adequately represent the national population.

Several factors have been associated with the occurrence of DR-TB in children. Most occurrences of DR-TB in children are due to transmission from intimate household contacts, and thus, a history of interaction with a DR-TB patient is an important risk factor[15]. In addition, the incidence of DR-TB was positively linked with HIV infection, malnutrition, and previous TB therapy[16,17]. Sociodemographic characteristics such as age, place of residence, educational level of the head of the household, exposure to tobacco, and environmental conditions have also been reported to influence the risk of tuberculosis infection and access to health services[18].

Although previous studies have explored pediatric DR-TB, nationally representative evidence regarding its prevalence and determinants in Indonesia remains scarce. Existing research has primarily focused on clinical characteristics and treatment outcomes, with limited attention to the combined influence of sociodemographic factors, treatment adherence, treatment supervision, household TB contact, nutritional status, smoking exposure, and environmental conditions. In addition, incomplete national data regarding socioeconomic and household environmental factors have limited accurate estimation of pediatric DR-TB prevalence and hindered comparisons across studies. Considering the complex interaction between biological, behavioral, social, and environmental determinants of DR-TB, a comprehensive population-based analysis is needed to understand pediatric DR-TB in Indonesia better[19].

Therefore, this study aimed to estimate the prevalence of drug-resistant TB among children in Indonesia and to identify factors associated with its occurrence using data from the 2023 Indonesian Health Survey. The findings are expected to support evidence-based policy development and strengthen national TB control strategies for children.

2. Methods

2.1. Data sources

This study utilized secondary data from the 2023 Indonesian Health Survey, a cross-sectional integrated survey combining the Basic Health Research and the Indonesia Toddler Nutrition Status Survey, covering 38 provinces and 514 districts/cities across Indonesia. Sampling was stratified at the census block and household levels to ensure national representativeness. Census blocks were selected using probability proportional to size (PPS) based on the 2020

Population Census, followed by systematic household sampling stratified by household head education. Of 34 500 selected census blocks, 34 065 (98.74%) were successfully surveyed. Overall, 315 646 general households, 284 178 households with children under five, and 1 191 692 individuals were interviewed. The study population included children aged 0-14 years from the 2023 Indonesian Health Survey, and the analytic sample consisted of 423 children diagnosed with TB by a physician. Details of participant selection are presented in Figure 1.

2.2. Variables and instruments

This study used variables from the household and individual questionnaires of the 2023 Indonesian Health Survey. Variables were chosen based on their clinical and epidemiological relevance reported in previous studies of DR-TB in children and other related risk factors of TB. These variables included known individual characteristics, household exposures, socio-demographic factors, and socio-economic conditions affecting the incidence of DR-TB in children[15,18]. Moreover, all identified variables were present in the study dataset and thus could be incorporated into the analysis.

The dependent variable was DR-TB, categorized as yes or no, based on physician diagnosis confirmed through probing of diagnoses at health care facilities. Independent variables included sociodemographic factors, TB treatment, TB treatment adherence, treatment supporter (directly observed therapy), household contact with TB patients, nutritional status, household smoking exposure, housing conditions, and contact with DR-TB patients.

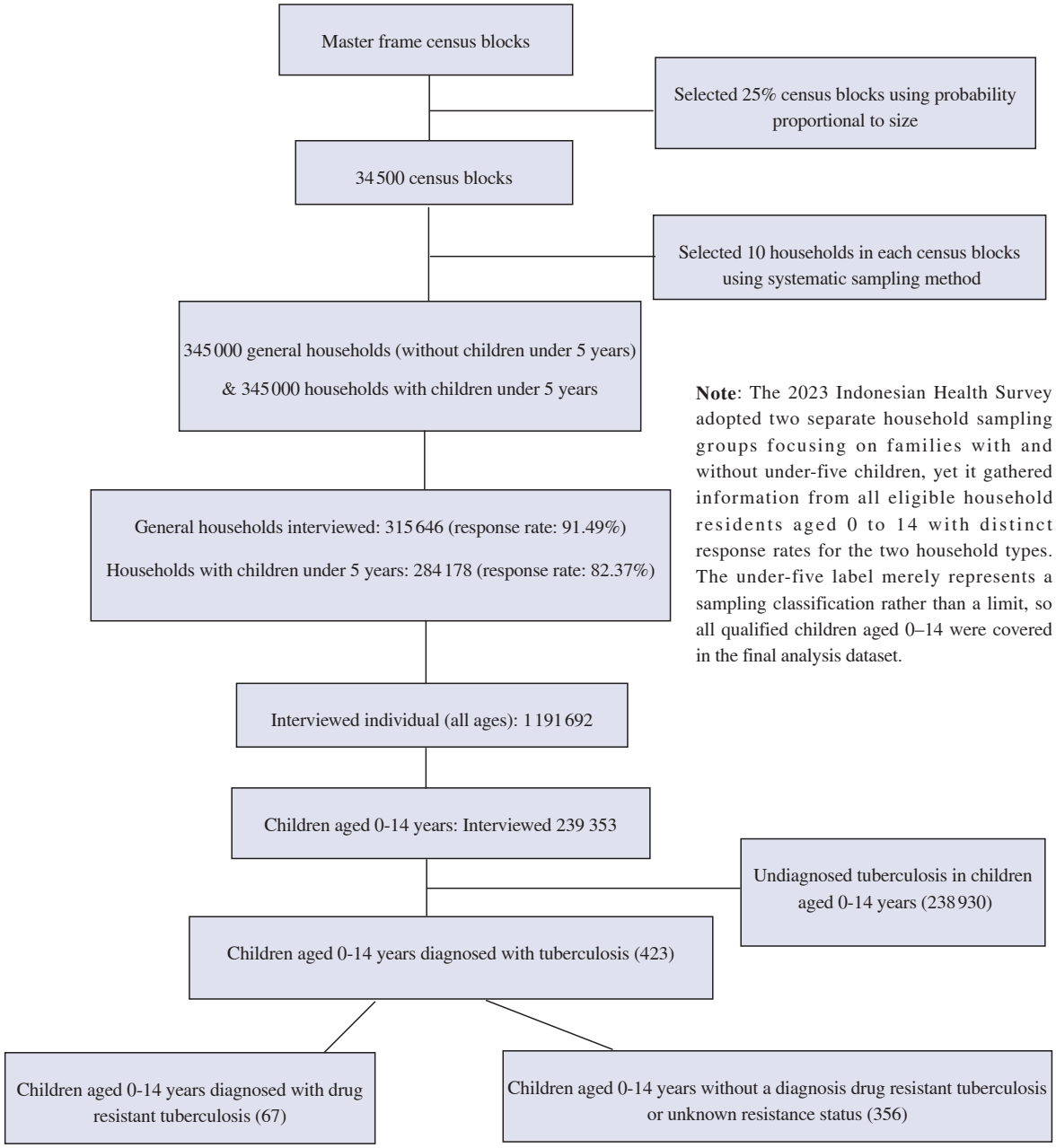


Figure 1. Selection of research subjects.

Sociodemographic factors comprised age group (<1 year, 1-4 years, and 5-14 years), sex (female, male), place of residence (urban, rural), household head's education level (Higher, No formal education or did not complete primary school, primary, secondary), and the household wealth index based on expenditure quintiles. According to the BPS classification, households were ranked into five expenditure quintiles (Q1-Q5) from the lowest to the highest level of per capita expenditure. For this study, the quintiles were grouped into three categories: poor (Q1-Q2), middle (Q3-Q4), and rich (Q5).

Treatment history was defined as the type of TB treatment previously received by children diagnosed with TB, as documented by the attending physician. The study categorized the TB treatment variable into four groups: Did not receive therapy, oral anti-tuberculosis drugs (ATD), injectable ATD, and combined oral and injectable ATD. Oral ATD included fixed-dose combinations (FDC), loose combination packs (Kombipak), and loose TB drugs. FDC refers to a combination of multiple anti-TB drugs in a single tablet, while Kombipak and loose formulations contain similar drug components; however, Kombipak is provided free through government programs, whereas loose drugs are obtained *via* paid prescriptions. Injectable ATD consisted of streptomycin as part of the combination anti-TB therapy.

TB treatment adherence was categorized as adherent or non-adherent based on regular completion of a six-month TB treatment regimen without interruption, as per physician instructions. The treatment supporter (directly observed treatment, DOT) variable was categorized as yes/no, defined as an individual trusted to supervise patients in taking medications at the correct dose and schedule until treatment completion. Treatment supporters may include family members, neighbors, community health volunteers, community leaders, or health workers.

Household contact with TB patients was categorized as yes or no and defined as living in the same household with a bacteriologically confirmed TB patient, as reported by the child's caregiver or parent. Nutritional status was assessed using body mass index-for-age and categorized as underweight (≥ −3 SD to < −2 SD), normal (≥ −2 SD to ≤ +1 SD), overweight (> +1 SD to ≤ +2 SD), or obese (> +2 SD), according to the WHO growth reference, with height and weight measured by trained enumerators.

Household smoking exposure was categorized as yes or no and defined as the presence of smoking by one or more household members inside the home. This information was obtained through a questionnaire-based interview that asked about lifetime smoking habits among all domestic workers aged 10 and older, including both current and former smokers. Housing conditions were classified as healthy housing or unhealthy housing. A healthy house was defined as meeting all criteria, including permanent roofing, ceiling, permanent walls, non-earthen flooring, adequate occupancy density (≥8 m^2 per person), electrical lighting, clean cooking fuel, and absence of household members smoking inside the home.

Household contact with DR-TB patients was categorized as yes or no, defined as living in the same household with a physician-diagnosed DR-TB patient based on caregiver interview.

2.3. Data analysis

We conducted a descriptive analysis to estimate the prevalence of DR-TB among children in each province of Indonesia. We used sample weights to obtain a nationally representative estimate. The bivariate associations between DR-TB and each independent variable were assessed by a *Chi*-square test. Variables with a *P*-value <0.25 in the bivariate analysis and factor considered as an epidemiologically important covariates based on prior evidence and its potential role as a confounder were considered for inclusion in the multivariable logistic regression model[20]. Then, multivariable logistic regression was performed to identify factors independently associated with DR-TB in children.

2.4. Ethical statement

The 2023 Indonesian Health Survey collected data through face-to-face interviews after obtaining voluntary informed consent from all respondents. Interviews with children younger than 15 years were conducted in the presence of a parent or legal guardian. The survey 2023 protocol was approved by the Health Research Ethics Committee. In addition, this secondary data analysis received ethical approval from the Health Research Ethics Committee of the National Research and Innovation Agency (BRIN), Indonesia (Approval No. 054/KE.03/SK/03/2024; March 11, 2024).

3. Results

Figure 2 illustrates the distribution of DR-TB prevalence among children in Indonesia in 2023, ranging from <0.0001% to >41.90%, with a national prevalence of 15.94%. The highest prevalence was observed in East Kalimantan, West Kalimantan, and DKI Jakarta, with variation across provinces in Java, Kalimantan, Sulawesi, Maluku, Papua, Sumatra, Bali, and Nusa Tenggara.

Table 1 summarizes the baseline characteristics of the 423 study participants. Most participants were aged 5-14 years (48.2%), male (61.9%), and resided in urban areas (66.7%). Secondary education was the most common educational level of the household head (32.6%), and 42.1% of participants belonged to the middle wealth index category. Most children received ATD therapy (69.7%), had a medication supervisor (68.8%), and were adherent to TB treatment (73.8%). The majority had no household TB contact (86.5%), had normal nutritional status (73.5%), lived in unhealthy homes (66.2%), and had no household contact with DR-TB patients (96.5%).

Table 1. Baseline sociodemographic, clinical, and household characteristics of the study participants (*N*=423).

Variable	*n* (%)
Age	
<1 year	97 (22.9)
1-4 years	122 (28.9)
5-14 years	204 (48.2)
Sex	
Female	161 (38.1)
Male	262 (61.9)
Place of residence	
Urban	282 (66.7)
Rural	141 (33.3)
Household head's educational level	
Higher	98 (23.2)
No formal education or did not complete primary school	115 (27.2)
Primary	72 (17.0)
Secondary	138 (32.6)
Wealth index*	
Rich	144 (34.0)
Poor	101 (23.9)
Middle	178 (42.1)
Type of TB treatment	
Did not receive therapy	123 (29.1)
Oral ATD	295 (69.7)
Injectable ATD	2 (0.5)
Combined oral and injectable ATD	3 (0.7)
Treatment supporter	
No	132 (32.2)
Yes	291 (68.8)
TB treatment adherence	
Adherent	312 (73.8)
Non-adherent	111 (26.2)
Household TB contact	
No	366 (86.5)
Yes	57 (13.5)
Nutritional status	
Normal weight	311 (73.5)
Underweight	46 (10.9)
Overweight	40 (9.6)
Obesity	26 (6.0)
Household smoking exposure	
No	228 (53.9)
Yes	195 (46.1)
Housing condition#	
Healthy housing	143 (33.8)
Unhealthy home	280 (66.2)
Household contact with DR-TB patients	
No	408 (96.5)
Yes	15 (3.5)
Total	423 (100.0)

ATD: oral anti-tuberculosis drug; DR-TB: drug-resistant tuberculosis; *poor (Q1-Q2), middle (Q3-Q4), and rich (Q5) according to the BPS classification, which ranks household into five expenditure quintiles (Q1-Q5) from the lowest to the highest level of per capita expenditure. #A healthy house was defined as meeting all criteria, including permanent roofing, ceiling, permanent walls, non-earthen flooring, adequate occupancy density (≥8 m² per person), electrical lighting, clean cooking fuel, and absence of household members smoking inside the home.

Table 2 shows that, based on bivariate analysis, variables significantly associated with DR-TB among children in Indonesia included place of residence, TB treatment regimen, presence of a treatment supporter, medication adherence, nutritional status, and household contact with drug-resistant TB patients (P<0.05). The prevalence of DR-TB was higher among children living in urban areas (19.6%), most received a combination of oral and injectable anti-TB therapy (70.6%), had a treatment supporter (19.4%), were adherent to TB treatment (19.6%), and had either underweight (25%) or an overweight status (38%). In addition, the majority had household contact with DR-TB patients (95.2%).

Table 3 presents the results of the multivariable logistic regression analysis. Place of residence, wealth index, TB treatment adherence, household TB contact, and household contact with DR-TB patients were significantly associated with the odds of DR-TB (overall P< 0.05). Children living in rural areas (a*OR* 2.680; 95% *CI* 1.230-5.839), those with poor TB treatment adherence (a*OR* 17.353; 95% *CI* 3.098-97.206), and those with household TB contact (a*OR* 5.628; 95% *CI* 1.113-28.450) had significantly higher odds of DR-TB. Although the wealth index was significantly associated with DR-TB overall (P=0.018), neither the middle wealth group (a*OR* 0.714; 95% *CI* 0.292-1.749) nor the rich wealth group (a*OR* 1.939; 95% *CI* 0.724-5.188) differed significantly from the poor wealth group after adjustment. Conversely, children with household contact with DR-TB patients had significantly lower odds of DR-TB than those without such contact (a*OR* 0.001; 95% *CI* 0.000-0.014).

4. Discussion

The prevalence of DR-TB among Indonesian children in 2023 showed substantial geographic variation. Provinces in Java, parts of Kalimantan, Sulawesi, and Papua demonstrated higher prevalence levels, indicating a greater burden of pediatric DR-TB in these regions. In contrast, many provinces in Sumatra and Nusa Tenggara, and several eastern islands, were classified as having lower prevalence. These spatial findings reveal clear interprovincial disparities and suggest that the distribution of pediatric DR-TB is heterogeneous at the national level, likely reflecting differences in health system capacity, access to timely diagnosis and treatment, treatment adherence, and underlying socioeconomic conditions. These findings highlight the need for targeted, province-specific strategies to strengthen TB control and drug-resistance surveillance among children, particularly in high-burden areas.

Multivariable analysis showed that children living in rural areas had a higher risk of developing DR-TB compared with those living in urban areas. These findings are in line with the global body of evidence indicating significant healthcare disparities between rural and urban populations, particularly in terms of access to and

Table 2. Bivariate analysis of factors associated with DR-TB among children in Indonesia (*N*=423).

Predictor	DR-TB in children, *n* (%)		χ^2 values	*P* value
	Yes	No		
Age			2.867	0.350
< 1 year	13 (13.9)	84 (86.1)		
1-4 years	15 (12.4)	107 (87.6)		
5-14 years	39 (19.0)	165 (81.0)		
Sex			1.317	0.302
Female	21 (13.3)	140 (86.7)		
Male	46 (17.5)	216 (82.5)		
Place of residence			8.493	<0.001
Urban	55 (19.6)	227 (80.4)		
Rural	12 (8.6)	129 (91.4)		
Household head's educational level			2.576	0.602
Higher	10 (10.9)	87 (89.1)		
No formal education or did not complete primary school	20 (17.2)	95 (82.8)		
Primary	14 (19.1)	59 (80.9)		
Secondary	23 (16.8)	115 (83.2)		
Wealth index			3.853	0.254
Poor	16 (15.8)	85 (84.2)		
Middle	35 (19.6)	144 (80.4)		
Rich	16 (11.5)	127 (88.5)		
Type of TB treatment			21.547	<0.001
Did not receive therapy	7 (5.6)	116 (94.4)		
Oral ATD	58 (19.7)	237 (80.3)		
Injectable ATD	0 (0.0)	2 (100.0)		
Combined oral and injectable ATD	2 (70.6)	1 (29.4)		
Treatment suporter			8.131	0.007
No	11 (8.4)	121 (91.6)		
Yes	56 (19.4)	235 (80.6)		
TB treatment adherence			12.159	<0.001
Adherent	61 (19.6)	251 (80.4)		
Non-adherent	6 (5.5)	105 (94.5)		
Household TB contact			6.339	0.154
No	52 (14.2)	314 (85.8)		
Yes	15 (27.3)	42 (72.7)		
Nutritional status			15.054	0.038
Normal weight	39 (12.5)	273 (87.5)		
Underweight	11 (25.0)	34 (75.0)		
Overweight	7 (18.0)	33 (82.0)		
Obesity	10 (38.0)	16 (62.0)		
Household smoking exposure			0.979	0.318
No	40 (17.6)	188 (82.4)		
Yes	27 (14.0)	168 (86.0)		
Housing condition			0.485	0.503
Healthy housing	20 (14.2)	123 (85.8)		
Unhealthy housing	47 (16.8)	233 (83.2)		
Household contact with DR-TB patients			71.354	<0.001
No	53 (13.1)	355 (86.9)		
Yes	14 (95.2)	1 (4.8)		
Total	67 (15.9)	356 (84.1)		

TB: tuberculosis; ATD: oral anti-tuberculosis drugs; DR-TB: drug-resistant tuberculosis.

utilization of health services. This finding may be related to limited diagnostic services, delayed treatment initiation, and unequal drug distribution, which contribute to poor treatment adherence and increased risk of DR-TB[21]. A study conducted in South Africa found that social, economic, and environmental factors including poverty, overcrowding, malnutrition, and lower levels of education and employment in rural areas may increase the risk of TB infection and disease progression while limiting access to quality TB care[22]. A systematic review of studies conducted across multiple countries found that weak surveillance systems in rural areas may hinder timely contact tracing and index case reporting, thereby making community transmission of DR-TB more difficult to control[23].

Although the wealth index was significantly associated with DR-TB overall, no statistically significant differences were observed between the middle or rich wealth groups and the poor wealth group after adjustment for other covariates. These findings suggest that the relationship between socioeconomic status and DR-TB may be more complex than can be explained by household wealth categories

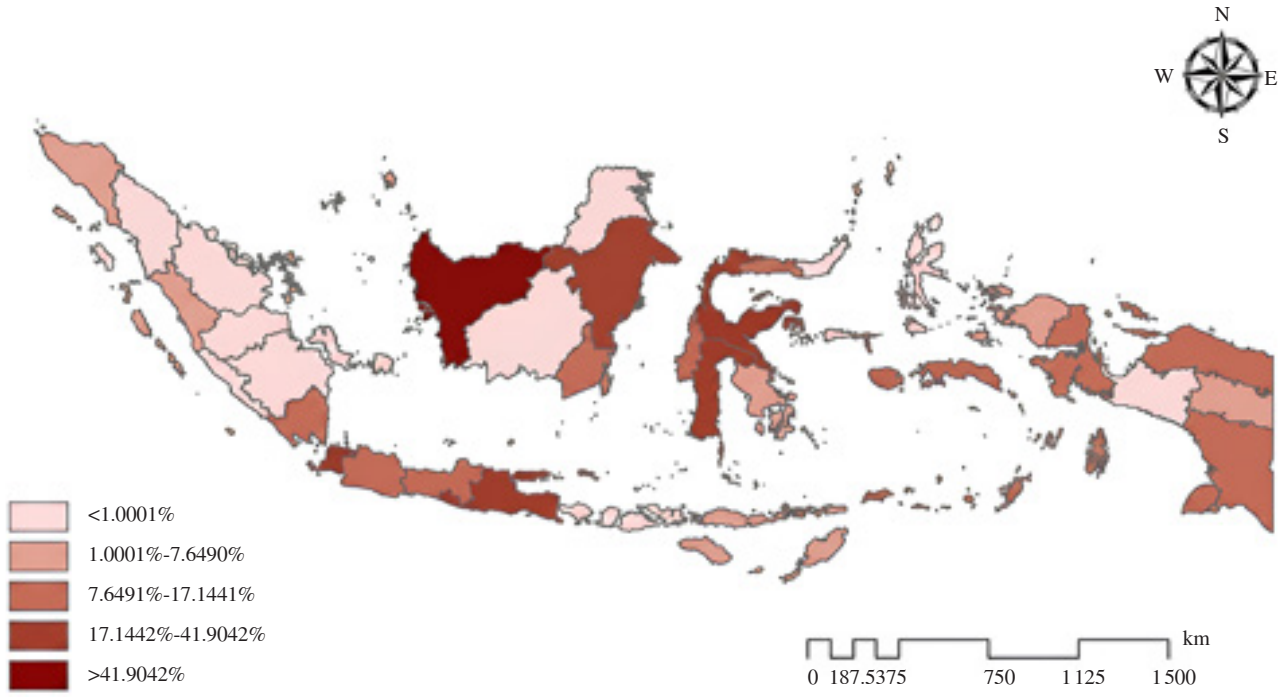


Figure 2. The prevalence of drug-resistant TB among children in Indonesia (n=423).

Table 3. Binary logistic regression analysis of DR-TB among children in Indonesia.

Variable	B	a*OR*	95% *CI*	*P* value
Place of residence				
Urban (ref)				
Rural	0.986	2.680	1.230-5.839	0.013
Wealth index				0.018
Poor (ref)				
Middle	-0.337	0.714	0.292-1.749	0.461
Rich	0.662	1.939	0.724 -5.188	0.187
TB treatment adherence				
Adherence (ref)				
Non adherence	2.854	17.353	3.098-97.206	0.001
Household TB contact				
No (ref)				
Yes	1.728	5.628	1.113-28.450	0.037
Household contact with DR-TB patients				
No (ref)				
Yes	-7.498	0.001	0.000-0.014	<0.001

a*OR*: Adjusted odds ratio; *CI*: Confidence interval.

alone. Unlike previous studies, which consistently reported an increased risk of TB and DR-TB among individuals with lower socioeconomic status due to limited access to healthcare, household overcrowding, and poor nutritional conditions[11,24-26]. our study did not observe statistically significant differences between wealth categories after adjustment. One possible explanation is that the wealth index used in this study may not fully capture access to TB care or treatment-seeking behavior. In addition, the relatively small number of DR-TB cases and the distribution of participants across wealth categories may have limited the statistical power to detect significant differences. Furthermore, the relationship between socioeconomic status and DR-TB is likely influenced by broader social determinants, health system characteristics, and patterns of community transmission[27]. Previous studies have also highlighted the importance of socioeconomic factors, including income, education, and social support, in shaping the burden of DR-TB globally[28,29].

The findings of this study showed that poor adherence to TB treatment was significantly associated with DR-TB. This result is consistent with existing evidence indicating that non-adherence to TB treatment regimens is a major determinant of drug resistance development. TB therapy requires regular and complete administration of combination anti-TB drugs for at least six months to eradicate *M. tuberculosis*. Previous studies have demonstrated that treatment non-adherence is a major driver of DR-TB, as inadequate and inconsistent drug exposure creates selective pressure that promotes the emergence and amplification of resistant *M. tuberculosis* strains[30,31]. Factors such as prolonged treatment duration, adverse

drug effects, limited social support, stigma, and restricted access to health services may contribute to treatment non-adherence[32,33]. The high odds ratio observed in this study further emphasizes the importance of strengthening treatment adherence through treatment supervision, family support, and improved health care services.

Children with a history of household contact with TB patients had approximately 5.6 times higher risk of developing DR-TB compared with those without household contact, highlighting the importance of household transmission in the epidemiology of DR-TB. *M. tuberculosis* is transmitted *via* aerosol droplets, and prolonged and close household exposure increases the likelihood of both latent and active infection, including drug-resistant strains. In endemic settings, households are a major site of TB transmission in low- and middle-income countries in Southeast Asia, with children representing a particularly vulnerable population[34]. A global meta-analysis demonstrated that children with household exposure to TB patients are at substantially higher risk of infection and progression to active TB. The risk is greatest among close contacts and increases with the intensity and duration of exposure, particularly during the early period following contact with an infectious index case[35,36]. A review of molecular epidemiological studies demonstrated that most childhood TB cases result from transmission by adult household members, particularly those residing in the same household[37]. A study in Ethiopia also reported an association between contact with TB-positive individuals and the risk of DR-TB, although effect sizes varied across populations[38]. The WHO emphasizes the importance of contact investigation and screening among children exposed to MDR/RR-TB cases for early diagnosis, given the high concordance of resistance patterns, particularly to isoniazid and rifampicin[39]. These findings indicate that household transmission plays a critical role in the epidemiology of DR-TB, underscoring the need for contact investigation, early screening, and preventive therapy in children to interrupt transmission chains.

This study found that contact with DR-TB patients was associated with extremely low odds of DR-TB in children. In contrast to our findings, the global literature consistently identifies close household contact with MDR-TB patients as a major determinant of pediatric MDR-TB[40]. This unexpected finding may be influenced by detection and surveillance bias resulting from intensive contact tracing and screening, which can facilitate earlier diagnosis and intervention[21]. It may also reflect differences in surveillance practices, follow-up duration, and case definitions, while enhanced monitoring and preventive therapy among DR-TB contacts could reduce or delay the detection of DR-TB cases[34,41]. In addition, the results may have been affected by limitations of secondary data, potential misclassification bias, the small number of participants in the DR-TB contact group leading to unstable and extreme odds ratio estimates, and possible reverse causality, whereby children already diagnosed with DR-TB may no longer have been classified as contacts[42-44]. Therefore, this finding does not reflect a true biological protective effect and should be interpreted cautiously in light of observational study limitations, underscoring the need for longitudinal research to assess causal relationships more accurately.

Overall, this study highlights the importance of rural residence, TB treatment adherence, and household TB contact as factors associated with pediatric DR-TB in Indonesia. Although the wealth index was associated with DR-TB overall, no significant differences were observed between individual wealth categories after adjustment. The unexpected inverse association between household contact with DR-TB patients and pediatric DR-TB should be interpreted cautiously because it may reflect surveillance bias, sparse data, or residual confounding rather than a true biological protective effect. Further longitudinal studies with larger sample sizes are needed to clarify these associations.

This study highlights the critical importance of adopting a multidimensional approach to DR-TB control, integrating medical interventions with efforts to address the underlying social and behavioral determinants that drive disease transmission and progression. These findings highlight the importance of strengthening early detection, contact tracing, monitoring of treatment adherence, and surveillance of DR-TB, particularly in regions with a high disease burden and limited access to health care services. In addition, improving access to rapid diagnostic testing, expanding community-based TB programs, and enhancing family-centered treatment support may help reduce transmission, improve treatment outcomes, and prevent the emergence of further drug resistance among children.

A key limitation of this study is that, although multivariable analyses were statistically significant, several odds ratios had wide confidence intervals due to a limited number of cases or imbalanced data distribution. In addition, the use of interview-based data without clinical verification may introduce misclassification bias, potentially affecting risk estimates; therefore, the findings should be interpreted cautiously within the studied population. Future studies should utilize prospective multicenter cohort designs with larger sample sizes and detailed assessments of household exposure to validate the observed protective effect of DR-TB contact. The incorporation of molecular epidemiological methods, such as whole-genome sequencing, is recommended to differentiate household from community transmission and to minimize residual confounding [31]. Additionally, future research should comprehensively evaluate socioeconomic, behavioral, environmental, and health-system factors that may influence the risk of pediatric DR-TB.

Conflict of interest statement

The authors declare that they have no conflict of interest.

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Authors' contributions

ZKN prepared a data set. RR analyzed the data, conceptualized and designed the study, and drafted the manuscript. RR, MM, HBN, IUT, ZKN and ADL participated in interpreting the results and commented on the manuscript. All authors have read and agreed to the published version of the manuscript. RR acts as the principal investigator.

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