

## Original Article

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## *Mycobacterium tuberculosis* infection among children under fifteen years of age: A population–based study in Indonesia

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### ABSTRACT

**Objective:** To assess the prevalence of *Mycobacterium (M.) tuberculosis* infection and its associated risks in children under fifteen years of age.

**Methods:** Based on secondary data from the 2018 Indonesian Basic Health Survey (RISKESDAS 2018), this cross-sectional study employed *M. tuberculosis* infection in children as a dependent variable and age level, sex, region, location, family case positive, and smoking as independent variables. Geospatial analysis was applied to show the prevalence of *M. tuberculosis* infection and multivariate regression was performed to analyze the risk factors of getting the infection among children under 15 years of age.

**Results:** Prevalence ranges of *M. tuberculosis* infection among children aged 0–14 years, babies (age <12 months), toddlers (age 12–59 months), and children aged between 5 and 14 years were 0.03% to 0.57%, 0% to 0.64%, 0% to 0.78%, and 0.01% to 0.53%, respectively in Indonesia. A high prevalence of *M. tuberculosis* infection among children under 15 years of age was found in Papua and other provinces, such as Kalimantan and Java. Contacting with tuberculosis family members was positively associated with *M. tuberculosis* infection in children as shown by multivariate logistic regression (*OR* 8.94; 95% *CI* 5.4–14.6, *P*<0.05).

**Conclusions:** Contacting with family member who has tuberculosis is related with *M. tuberculosis* infection among children in Indonesia. Therefore, screening the household for contact with tuberculosis patients is a preventive treatment for children.

**KEYWORDS:** Tuberculosis; Children; RISKESDAS; Indonesia

### 1. Introduction

Tuberculosis (TB) remains an important challenge for global health caused by the bacillus *Mycobacterium (M.) tuberculosis*, which is spread when people who are sick with TB expel bacteria into the air (e.g. by coughing). Geographically, in 2021, most people who developed TB were in the World Health Organization (WHO) regions of South-East Asia (45%), Africa (23%) and the Western Pacific (18%), with smaller proportions in the Eastern Mediterranean (8.1%), the Americas (2.9%) and Europe (2.2%)[1]. Indonesia is the second country with the highest number of TB cases in the world after India and is classified as one of the 10 high burden countries

#### Significance

Tuberculosis (TB) in children is a significant public health problem because it is a marker for recent transmission of TB. TB infection is more frequent in toddlers (aged 12–59 months) and it is associated with contact with adult TB case. Hence, knowing the prevalence of TB and its associated factor in children may help to understand the situation of TB in children and help to fight against this disease.

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for TB, HIV-associated TB, and drug-resistant TB[1,2]. WHO estimated that 7.5 million children aged 0-14 years are infected with *M. tuberculosis* each year, and 1-1.2 million children progress to active TB disease, more than half of whom are aged under 5 years[3]. In 2021, 4% of TB cases occurred among children less than 15 years of age in the United States[4]. TB exists in all countries and across all age groups. However, TB can be cured and prevented. TB in children and adolescents is often neglected by healthcare providers and can be challenging to diagnose and treat[5].

The incidence of TB cases in Indonesia is 354 per 100 000 population, meaning that out of every 100 000 people in Indonesia, 354 are suffering from TB[1]. In Indonesia, TB is not only affecting adults. Children, especially those under the age of fifteen, are also vulnerable to the disease. Symptoms of TB in children are coughing for more than three weeks, fever for more than two weeks, coughing up blood, weakness and no energy, loss of appetite, weight loss, night sweats and swollen lymph nodes. Infants and young children are more likely than older children and adults to develop life-threatening TB disease (e.g., disseminated TB, TB meningitis). Among children, the higher numbers of TB cases can be seen in children younger than five years old and in adolescents older than ten years of age[4], the mortality is highest among the very young (0-4 years of age) compared to any other age group[6].

Indonesian Basic Health Survey (RISKESDAS) 2018 showed that the prevalence of TB in children in Indonesia ranges from 0.1%-0.3%[7]. Inventory TB study in Indonesia showed that most TB cases occurred in the age group  $\geq 15$  (82%), while the remaining 18% were aged  $< 15$  years. The under-reporting rate of TB  $< 15$  years was 54%. Under-reporting of TB in some children are mainly from non-primary health care facilities (71%) like hospitals, clinics, practice doctors generally, and specialists whereas the rest are from primary health care facilities (19%)[8]. Indonesia targeting 63 746 cases of diagnosed and treated TB in children, and the provision of 1 129 015 Tuberculosis Preventive Treatment to toddlers with contact, HIV sufferers and other risk groups in 2024[9].

Risk factors leading to the development of TB disease have gained focus over the years. Children bear severe forms of TB in comparison to adults[1,10]. Since no tests are available to measure the progression of the disease, the associated risk factors can be advantageous to speculate the disease. Infection in children can occur due to several internal and external factors. Internal factors include sex, age, birthweight, Bacille Calmette-Guérin immunization, nutritional status, and external factors including environmental condition. like contact with TB patients, smoking behaviors, house conditions, and overcrowding[11-16].

A study in Pekalongan reported that there was an association between the incidence of population density with children's pulmonary tuberculosis ( $P < 0.001$ ), ventilation ( $P = 0.004$ ), the temperature of the room ( $P = 0.036$ ), density occupancy ( $P \leq 0.001$ )

and natural lighting ( $P = 0.016$ ). The results of multivariate analysis showed that the risk factors for the incidence of children's pulmonary tuberculosis were mother's knowledge ( $OR\ 2.918$ ; 95%  $CI\ 1.005-8.472$ ;  $P = 0.049$ ), density occupancy ( $OR\ 3.379$ ; 95%  $CI\ 1.212-9.417$ ;  $P = 0.020$ ), humidity ( $OR\ 3.236$ ; 95%  $CI\ 1.156-9.058$ ;  $P = 0.025$ ) and ventilation ( $OR\ 3.224$ ; 95%  $CI\ 1.182-8.797$ ;  $P = 0.022$ )[17]. There was a correlation between nutritional status and pulmonary tuberculosis in children in Indonesia[18].

Infection in children can occur due to several factors including a history of contact with families with TB sufferers and smoking behavior. Children who live at home with adult pulmonary TB sufferers are at high risk of being infected and sick with TB (household contact)[15,19-22]. The risk was higher for children living in the same family as a TB case ( $HR\ 2.15$ ; 95%  $CI\ 1.3-3.7$ ) than for children living in the same house but not belonging to the same family as the TB case ( $HR\ 1.51$ ; 95%  $CI\ 1.0-2.2$ )[23]. The duration of household contact with smear-positive adult TB patients of more than 6 hours per day is also a risk factor for TB among children[24]. Some studies even report that contact with a TB case is the most dominant risk factor of TB in children[14,25]. Children who live in smokers' environments are also more at risk of being infected with *M. tuberculosis*[26,27]. Other conditions in the house like ventilation, overcrowding, and house sanitation too associated with TB in children[10,14-16,25].

A lot of studies about risk factors for TB have been done, but studies on TB in children is still limited. The purpose of this manuscript is to present a population-based study on *M. tuberculosis* infection in children under 15 years of age in Indonesia. This study aims to assess the prevalence of TB and factors associated with *M. tuberculosis* infection in this specific age group. The novelty of this manuscript lies in its specific focus on *M. tuberculosis* infection among children under fifteen in Indonesia, adopting a population-based approach because RISKESDAS implemented at 514 districts across 34 provinces in Indonesia (nationally representative health survey) to population based and providing valuable insights and strategies for tackling the disease burden in this vulnerable population.

## 2. Subjects and methods

### 2.1. Study design

This is a cross-sectional study of children under fifteen among 514 districts across 34 provinces in Indonesia. The primary data source was the RISKESDAS 2018, which is a nationally representative health survey that collects information on TB. Data is accessible with specific requirements and procedures through [www.badankebijakan.kemkes.go.id](http://www.badankebijakan.kemkes.go.id). Data can be accessed by sending email to [datin.bkpk@kemkes.go.id](mailto:datin.bkpk@kemkes.go.id).

RISKESDAS surveyed 300 000 households from 30 000 census blocks through a two-stage sampling process. Firstly, the survey team selected 180 000 census blocks out of the 720 000 listed in the 2010 population census, using probability proportional to size. Secondly, they picked 30 000 census blocks each from urban and rural areas, again using probability proportional to size. To maintain the variation among households, the team chose ten households according to implicit stratification of the education levels of household heads. The team then interviewed each household member and assessed those who met the inclusion criteria. The response rate to interviews was high, at 95% across the country with a range from 85% in Papua province to 99% in Bangka Belitung province. The survey included a total sample of 1 017 290 people interviewed. For this study, a total sample of 303 507 children of 0-14 years old (48.2% girls and 51.8% boys) were included[7].

## 2.2. Independent variable

The study analysed five independent variables at the age level, namely sex, region, location, family case positive, and smoking. These five variables measured at RISKESDAS 2018, and have been linked to *M. tuberculosis* infection in children on the previous studies in Indonesia[11,15,16,26,28,29]. The provinces were classified into five regions: Sumatera, Java and Bali, Kalimantan, Sulawesi, and Papua/ Nusa Tenggara/Maluku. Location is classified into two categories of urban and rural. Family-positive cases are another family living at home with children 0-14 years old. Smoking behaviour includes children/another family smoking in the house.

## 2.3. Dependent variable

The dependent variable in this study was the *M. tuberculosis* infection in children under fifteen years old, measured as a numeric outcome. The related survey question was "In the last year, has [NAME] ever been diagnosed with lung TB by doctors/ nurses/ midwives?". Age categories are in three levels, baby (under 12 months), toddler (12-59 months) and child (5-14 years old).

## 2.4. Statistical analysis

This study employed both geospatial analysis and multivariate regression to analyse data from 34 provinces and 514 districts. Before analyses, all data were set for survey data considering strata and cluster. Weighting was carried out on all analysis. The provincial-level TB data were divided into quintiles using Quantum GIS (QGIS). Logistic regression was used to analyse the determinant of *M. tuberculosis* infection in children. The ORs were used because the prevalence of *M. tuberculosis* infection in children in Indonesia was less than 10%. Moreover, the dependent variable was a binary

response (yes and no response). In conducting the regressions, we employed ordinary least squares and examined the relationship between independent and dependent variables. We analysed the associations between exposure indicators, such as sex, region, location, family case positive, smoking, and *M. tuberculosis* infection outcome indicators were performed in IBM SPSS ver. 22 (IBM Corp.), using 5% as statistically significant.

## 2.5. Inform consent and ethical approval

All the member of the households interviewed in the RISKESDAS were explained about the detail of the survey and informed about the consent. Written informed consent was obtained from all participants for inclusion in the study. Informed consent statement was printed on the form that signed by the member of the households who agree to participate in the survey.

This research received ethical approval from the Health Research Ethics Commission of the Indonesian Research and Development Agency Number: LB.02.01/2/KE.267/2017, amendment Number: LB.02.01/2/KE.024/2018.

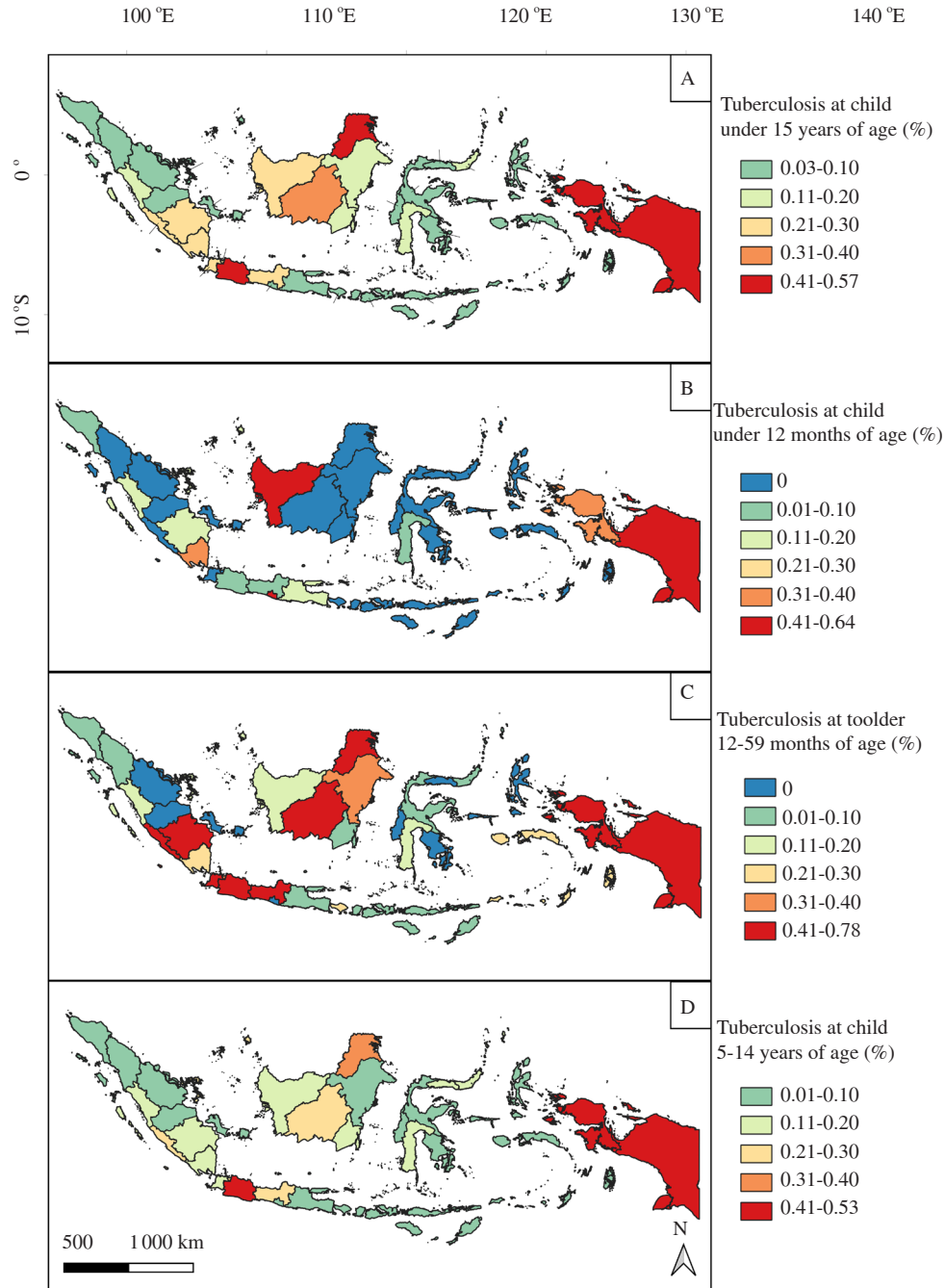
## 3. Results

### 3.1. Overview of TB prevalence in children

In Figure 1, the prevalence of TB in a child is shown by quintile at the provincial level. Panel A-D show the range of TB among all children, baby, toddler, and child with variants from 0.03% to 0.53%, 0% to 0.64%, 0% to 0.78%, and 0.01% to 0.53%, respectively. A high prevalence of TB among all children 0-14 years old was found in many provinces in Papua, and some provinces in other regions (e.g., Kalimantan and Java). The pattern for both childhood TB was relatively similar by category age.

Table 1 displays the frequency of childhood TB for each province. The bold cells signify that the prevalence in that province is higher than the national average (bottom row) for each outcome indicator. Overall, children aged 0-14 years in 10 provinces show a rate above the national rate (0.23%) and the highest is found in West Java (0.57%). Baby aged <12 months in seven provinces showed rates above the national rate (0.08%) and the highest was found in Yogyakarta (0.64%). Toddlers aged 12-59 months in 10 provinces show rates above the national rate (0.33%), and the highest is found in West Java (0.78%). Children aged 5-14 years in nine provinces show a rate above the national rate (0.21%), the highest in West Java province (0.53%). West Papua and Papua show rates above the national rate for all age groups.

Table 2 displays the prevalence of TB in childhood by sex, region, location, family case positive and smoking. The bold cells signify



**Figure 1.** Prevalence of tuberculosis by the province in Indonesia, 2018.

that the prevalence is higher than other categories in the group. According to sex variables, more girls were found TB positive in all age and child categories, while in babies and toddlers, prevalence was found higher in boys. In terms of the region variable, more TB were found in Java at all, toddler, and child categories, while babies are more commonly found in Kalimantan. The group of toddlers and children most found with TB lives in urban areas, while babies are more commonly found in rural areas. Children who live with other families who suffer from TB and smoke are also found to have TB in all age groups.

### 3.2. Factor associated with TB

Table 3 displays the association between childhood TB, sex, region, location, family case positive and smoking. Logistic regression analysis showed a relationship between children diagnosed with TB living in Java and household contacts with other families who were also diagnosed with TB ( $P < 0.05$ ). The risk of children living in Java is greater than that of children living outside Java ( $OR$  1.95; 95%  $CI$  1.9-2.8). Likewise, children who live with TB families have a greater chance of being infected with TB ( $OR$  8.94; 95%  $CI$  5.4-14.6).

**Table 1.** Prevalence of infection TB in children under 15 years of age by province in Indonesia, 2018 [*n* (%)].

| Province           | All                   | Baby                | Toddler               | Child                  |
|--------------------|-----------------------|---------------------|-----------------------|------------------------|
| Aceh               | 13 280 (0.09)         | 894 (0.07)          | 3 499 (0.09)          | 8 887 (0.09)           |
| North Sumatera     | 23 545 (0.08)         | 1 179 (0.00)        | 5 489 (0.10)          | 16 877 (0.08)          |
| West Sumatera      | 11 531 (0.15)         | 662 ( <b>0.12</b> ) | 2 831 (0.16)          | 8 038 (0.15)           |
| Riau               | 8 813 (0.04)          | 520 (0.00)          | 2 176 (0.00)          | 6 117 (0.06)           |
| Jambi              | 6 133 (0.07)          | 370 (0.00)          | 1 566 (0.00)          | 4 197 (0.10)           |
| South Sumatera     | 9 878 ( <b>0.26</b> ) | 537 (0.14)          | 2 463 ( <b>0.50</b> ) | 6 878 (0.18)           |
| Bengkulu           | 5 097 ( <b>0.29</b> ) | 314 (0.00)          | 1 258 ( <b>0.43</b> ) | 3 525 ( <b>0.26</b> )  |
| Lampung            | 9 117 (0.21)          | 586 ( <b>0.31</b> ) | 2 377 (0.25)          | 6 154 (0.18)           |
| Bangka Belitung    | 3 596 (0.05)          | 196 (0.00)          | 899 (0.00)            | 2 501 (0.07)           |
| Riau Islands       | 3 638 (0.20)          | 207 (0.11)          | 923 (0.14)            | 2 508 ( <b>0.24</b> )  |
| Jakarta            | 3 944 (0.26)          | 230 (0.00)          | 1 010 ( <b>0.40</b> ) | 2 704 ( <b>0.22</b> )  |
| West Java          | 20 774 (0.57)         | 1 259 (0.08)        | 5 352 ( <b>0.78</b> ) | 14 163 ( <b>0.53</b> ) |
| Central Java       | 23 184 (0.29)         | 1 500 (0.03)        | 5 864 ( <b>0.52</b> ) | 15 820 ( <b>0.23</b> ) |
| Yogyakarta         | 2 471 (0.10)          | 119 (0.64)          | 612 (0.00)            | 1 740 (0.09)           |
| East Java          | 23 076 (0.06)         | 1 443 (0.11)        | 5 832 (0.05)          | 15 801 (0.05)          |
| Banten             | 6 810 ( <b>0.25</b> ) | 430 (0.00)          | 1 755 ( <b>0.47</b> ) | 4 625 (0.19)           |
| Bali               | 4 969 (0.08)          | 285 (0.00)          | 1 185 (0.30)          | 3 499 (0.01)           |
| West Nusa Tenggara | 6 483 (0.06)          | 431 (0.00)          | 1 718 (0.06)          | 4 334 (0.07)           |
| East Nusa Tenggara | 16 352 (0.05)         | 924 (0.00)          | 3 900 (0.03)          | 11 528 (0.06)          |
| West Kalimantan    | 8 605 (0.21)          | 504 ( <b>0.55</b> ) | 2 112 (0.17)          | 5 989 (0.19)           |
| Central Kalimantan | 6 811 ( <b>0.35</b> ) | 403 (0.00)          | 1 683 ( <b>0.59</b> ) | 4 725 ( <b>0.29</b> )  |
| South Kalimantan   | 6 755 (0.11)          | 428 (0.00)          | 1 659 (0.10)          | 4 668 (0.13)           |
| East Kalimantan    | 5 571 (0.13)          | 330 (0.00)          | 1 407 (0.31)          | 3 834 (0.07)           |
| North Kalimantan   | 2 569 ( <b>0.41</b> ) | 174 (0.00)          | 688 ( <b>0.71</b> )   | 1 707 ( <b>0.33</b> )  |
| North Sulawesi     | 6 771 (0.11)          | 383 (0.00)          | 1 606 (0.09)          | 4 782 (0.13)           |
| Central Sulawesi   | 6 986 (0.07)          | 427 (0.00)          | 1 694 (0.04)          | 4 865 (0.08)           |
| South Sulawesi     | 15 169 (0.11)         | 907 (0.07)          | 3 636 (0.13)          | 10 626 (0.11)          |
| Southeast Sulawesi | 7 976 (0.03)          | 536 (0.00)          | 1 949 (0.00)          | 5 491 (0.05)           |
| Gorontalo          | 3 205 (0.09)          | 175 (0.00)          | 799 (0.00)            | 2 231 (0.14)           |
| West Sulawesi      | 3 734 (0.05)          | 226 (0.00)          | 854 (0.00)            | 2 654 (0.07)           |
| Maluku             | 7 028 (0.08)          | 417 (0.00)          | 1 695 (0.22)          | 4 916 (0.03)           |
| North Maluku       | 5 474 (0.05)          | 280 (0.00)          | 1 334 (0.00)          | 3 860 (0.08)           |
| West Papua         | 5 282 (0.48)          | 347 (0.36)          | 1 427 (0.48)          | 3 508 (0.50)           |
| Papua              | 8 880 (0.45)          | 471 (0.41)          | 2 274 (0.53)          | 6 135 (0.43)           |
| Average            | 303 507 (0.23)        | 18 094 (0.08)       | 75 526 (0.33)         | 209 887 (0.21)         |

All: children aged 0-14 years; baby: age<12 month; toddler: age 12-59 months; child: age 5-14 years. Bold values show values higher than the national average for each group.

**Table 2.** Prevalence of TB children under 15 years of age by sex, region, location, family case positive and smoking in Indonesia, 2018 [*n* (%)].

| Variables            |                | All                     | Baby                   | Toddler                | Child                   |
|----------------------|----------------|-------------------------|------------------------|------------------------|-------------------------|
| Sex                  | Boys           | 157 490 (0.23)          | 9 242 ( <b>0.10</b> )  | 39 317 ( <b>0.35</b> ) | 108 931 (0.20)          |
|                      | Girls          | 146 017 ( <b>0.24</b> ) | 8 852 (0.06)           | 36 209 (0.32)          | 100 956 ( <b>0.22</b> ) |
| Region               | Sumatera       | 94 628 (0.14)           | 5 465 (0.08)           | 23 481 (0.17)          | 65 682 (0.13)           |
|                      | Java           | 85 228 ( <b>0.32</b> )  | 5 266 (0.07)           | 21 610 ( <b>0.47</b> ) | 58 352 ( <b>0.28</b> )  |
|                      | Kalimantan     | 30 311 (0.20)           | 1 839 ( <b>0.17</b> )  | 7 549 (0.28)           | 20 923 (0.17)           |
|                      | Sulawesi       | 43 841 (0.09)           | 2 654 (0.03)           | 10 538 (0.07)          | 30 649 (0.10)           |
| Papua                |                | 49 499 (0.15)           | 2 870 (0.08)           | 12 348 (0.17)          | 34 281 (0.15)           |
|                      | Urban          | 120 889 ( <b>0.27</b> ) | 7 124 (0.07)           | 30 557 ( <b>0.42</b> ) | 83 208 ( <b>0.23</b> )  |
| Rural                | 182 618 (0.19) | 10 970 ( <b>0.09</b> )  | 44 969 (0.22)          | 126 679 (0.19)         |                         |
| Family case positive | Yes            | 3 583 ( <b>1.92</b> )   | 194 ( <b>1.65</b> )    | 859 ( <b>2.73</b> )    | 2 530 ( <b>1.64</b> )   |
|                      | No             | 299 924 (0.21)          | 17 900 (0.06)          | 74 667 (0.30)          | 207 357 (0.19)          |
| Smoking              | Yes            | 222 240 ( <b>0.24</b> ) | 13 819 ( <b>0.09</b> ) | 55 973 ( <b>0.35</b> ) | 152 448 ( <b>0.21</b> ) |
|                      | No             | 81 267 (0.21)           | 4 275 (0.04)           | 19 553 (0.26)          | 57 439 (0.20)           |
| Average              |                | 303 507 (0.23)          | 18 094 (0.08)          | 75 526 (0.33)          | 209 887 (0.21)          |

Java region includes Bali; Papua region includes Maluku and Nusa Tenggara; baby: age<12 months; toddler: age: 12-59 months; child: age 5-14 years. Bold values show values higher than other categories in the group. The 34 provinces were classified into five regions: Sumatera, Java and Bali, Kalimantan, Sulawesi, and Papua/Nusa Tenggara/Maluku. Location is classified into two categories of urban and rural.

**Table 3.** Regression output sex, region, location, family case positive and smoking in Indonesia, 2018.

| Variables             |            | All   |              | Baby   |               | Toddler |              | Child |              |
|-----------------------|------------|-------|--------------|--------|---------------|---------|--------------|-------|--------------|
|                       |            | OR    | 95% CI       | OR     | 95% CI        | OR      | 95% CI       | OR    | 95% CI       |
| Bivariate analysis    |            |       |              |        |               |         |              |       |              |
| Sex                   | Boys       | 0.97  | 0.746-1.263  | 1.57   | 0.426-5.755   | 1.09    | 0.701-1.702  | 0.88  | 0.633-1.234  |
|                       | Girls      | Ref.  |              |        |               |         |              |       |              |
| Region                | Sumatera   | 0.89  | 0.568-1.408  | 1.03   | 0.163-6.432   | 1.01    | 0.463-2.208  | 0.83  | 0.502-1.384  |
|                       | Java       | 2.08* | 1.427-3.020  | 0.86   | 0.130-5.677   | 2.82*   | 1.511-5.256  | 1.82* | 1.129-2.931  |
|                       | Kalimantan | 1.31  | 0.836-2.061  | 2.08   | 0.170-25.505  | 1.65    | 0.787-3.442  | 1.12  | 0.637-1.962  |
|                       | Sulawesi   | 0.56  | 0.337-0.929  | 0.35   | 0.029-4.246   | 0.44    | 0.169-1.145  | 0.63  | 0.340-1.153  |
| Location              | Papua      | Ref.  |              |        |               |         |              |       |              |
|                       | Urban      | 1.39* | 1.073-1.793  | 0.83   | 0.395-13.199  | 1.88*   | 1.222-2.895  | 1.17  | 0.847-1.616  |
| Family case positive  | Rural      | Ref.  |              |        |               |         |              |       |              |
|                       | Yes        | 9.23* | 5.719-14.907 | 27.89* | 5.468-142.218 | 9.28*   | 4.175-20.651 | 8.70* | 5.188-14.590 |
| Smoking               | No         | Ref.  |              |        |               |         |              |       |              |
|                       | Yes        | 1.16  | 0.855-1.568  | 2.28   | 0.395-13.199  | 1.34    | 0.801-2.228  | 1.05  | 0.728-1.518  |
|                       | No         | Ref.  |              |        |               |         |              |       |              |
|                       | Yes        | 1.16  | 0.855-1.568  | 2.28   | 0.395-13.199  | 1.34    | 0.801-2.228  | 1.05  | 0.728-1.518  |
| Multivariate analysis |            |       |              |        |               |         |              |       |              |
| Sex                   | Boys       | 0.96  | 0.738-1.252  | 1.45   | 0.403-5.201   | 1.11    | 0.709-1.731  | 0.87  | 0.622-1.220  |
|                       | Girls      | Ref.  |              |        |               |         |              |       |              |
| Region                | Sumatera   | 0.89  | 0.566-1.401  | 1.12   | 0.174-7.234   | 0.97    | 0.447-2.096  | 0.85  | 0.509-1.411  |
|                       | Java       | 1.95* | 1.948-2.832  | 0.89   | 0.101-7.843   | 2.38*   | 1.274-4.432  | 1.81* | 1.131-2.909  |
|                       | Kalimantan | 1.30  | 0.831-2.050  | 2.29   | 0.117-29.614  | 1.55    | 0.737-3.250  | 1.14  | 0.650-2.009  |
|                       | Sulawesi   | 0.54  | 0.325-0.896  | 0.35   | 0.028-4.335   | 0.41    | 0.158-1.072  | 0.61  | 0.333-1.130  |
| Location              | Papua      | Ref.  |              |        |               |         |              |       |              |
|                       | Urban      | 1.15  | 0.881-1.496  | 0.87   | 0.166-4.594   | 1.49    | 0.952-2.325  | 0.98  | 0.712-1.359  |
| Family case positive  | Rural      | Ref.  |              |        |               |         |              |       |              |
|                       | Yes        | 8.94* | 5.462-14.653 | 27.57* | 5.628-135.103 | 8.67*   | 3.738-20.098 | 8.54* | 5.057-14.416 |
| Smoking               | No         | Ref.  |              |        |               |         |              |       |              |
|                       | Yes        | 1.11  | 0.816-1.511  | 2.30   | 0.393-13.486  | 1.25    | 0.741-2.117  | 1.02  | 0.700-1.472  |
|                       | No         | Ref.  |              |        |               |         |              |       |              |
|                       | Yes        | 1.11  | 0.816-1.511  | 2.30   | 0.393-13.486  | 1.25    | 0.741-2.117  | 1.02  | 0.700-1.472  |

Java region includes Bali; Papua region includes Maluku and Nusa Tenggara; baby: age<12 months; toddler: age: 12-59 months; child: age 5-14 years; Bivariate and multivariate analyses were conducted using regressions in SPSS version 22. Asterisk (\*) indicates statistical significance at a 5% level or lower.

## 4. Discussion

### 4.1. Prevalence TB children

The result showed that prevalence of TB in children under 15 years of age is 0.23% with the highest prevalence found in children under 5 years of age (0.33%). The same result was shown on the previous RISKESDAS where the prevalence of TB in children under five years of age was higher compare to other children age group (0.4%)[30]. In addition, the mortality of TB is highest among 0-4 years of age compared to any other group[6].

The prevalence of TB in Indonesia is 0.42%[7], the same as the previous RISKESDAS[30]. Likewise, the province with the highest prevalence was West Java[7,30]. Indonesia targets TB elimination at all ages of 190/100 000 people by 2024 and 65/100 000 people by 2030[9]. Another study showed that the proportion of child TB cases in 22 countries with a high burden of TB, including Indonesia, ranges from 4%-21% of total TB cases[31]. Children have a higher risk of contracting TB and other pulmonary diseases than adults[29]. The rate of TB in children aged 0-5 years old was 3.5 times higher than the rate in adults and other children age group[32]. Children with *M. tuberculosis* infection have a higher chance of developing active TB disease because their immune system is not as developed as an

adult's immune system[33]. Moreover their immune systems are not yet optimal and very vulnerable to infection[34]. However, children have a lower risk than adults of developing drug-resistant forms of TB due to inappropriate treatment[29].

Another study showed more children with TB found at age 5-14 years old because children in this age group already know the world outside the home, so the possibility of having contact with positive adult TB sufferers is greater. In the age group of 5-14 years, children are exposed to many people outside their homes including positive adult TB sufferers, which is a major factor in transmitting TB to children[28]. In 2018, tuberculosis was found in up to 56% of children under 5 years in Brazil, affected by helminth coinfection, malaria, chronic viral infections, live attenuated virus vaccines, and hypovitaminosis D[35].

TB in children under fifteen was found to be more common in girls than boys, because girls are more susceptible than males to TB[36], as reported in Mumbai, India[37]. In most countries, more male than female cases of tuberculosis are reported[1]. Globally, preventive treatment of tuberculosis in children is underutilized. Treatment must be scaled up to help eliminate clusters of *M. tuberculosis* infection and achieve the goals of the End TB Strategy[38]. Diagnostic methods and management systems for tuberculous meningitis (TBM) in children are difficult to implement, resulting in higher rates of death, neurological disability, and morbidity[39].

#### 4.2. Factors associated with TB in children

The result of the bivariate analysis showed that TB in children was related to living in region of Java, urban areas and living with family-positive cases. RISKESDAS reported that the region Java is the area with the most TB cases compared to the other regions in Indonesia[7]. Urban areas have more TB than rural areas in some countries because a high proportion of urban residents in some low- and middle-income countries live in dismal conditions that favour the transmission of many diseases, including TB. An extreme manifestation of such poor living conditions in slums is defined by overcrowding, lack of water and sanitation, lack of secure tenure, and poor quality of housing[40]. The effect of urbanization on TB burden is mixed, compared to rural areas, TB case notification rates (CNRs) in urban and peri-urban areas reflect a high TB burden in urban areas[1]. Although high urban TB CNRs can be misleading because of cases coming from outside city[41].

Based on the result of multivariate analysis, only family cases were positively associated with TB in children. Children who live with a family with cases are more likely to develop TB than those who live with non-family cases. The risk of contracting TB was higher for children living with family with a TB case than children who living without TB case[23]. A study in North Sumatra showed the duration of household contact with smear-positive adult TB patients of more than 6 hours per day are risk factors for developing TB among children[24]. Children <5 years of age at Guinea-Bissau exposed to an adult with intrathoracic TB had 66% higher mortality than unexposed children (*HR* 1.66; 95% *CI* 1.2-2.3), family contact with a TB case represents a significant risk factor for child mortality in low-income countries[23]. Similarly, a study in Gambia showed that the risk of *M. tuberculosis* infection in a child increased with the proximity of the child to the individual with TB within the household and with the degree of activities shared with the individual with TB[42]. The most recent study in Ethiopia showed that a history of tuberculosis contact was associated with *M. tuberculosis* infection in children aged <15 years old ( $P \leq 0.001$ ; aOR 14.78; 95% *CI* 4.43-49.26)[43].

A systematic review and meta-analysis of 14 kinds of the literature showed that contact with known TB cases was associated with TB in children (*OR* 6.42; 95% *CI* 3.85-10.71)[25]. Two studies at Central Java showed similar results (*OR* 6.01; 95% *CI* 1.36-26.39)[16], and (*OR* 5.54; 95% *CI* 1.49-20.61)[15]. A study at Ambon City showed a higher risk (*OR* 31)[28]. A Nigeria study showed that TB in children was associated with contact history with adult TB patients too (*OR* 2.91)[10]. A study in Peru (2009-2012) on 4545 children between 0-14 years old who have been exposed to family TB cases within one year showed, 156 (3.4%) were diagnosed with TB (3.4%, 2.3%, and 4.7% in children aged 0-4, 5-9, and 10-14 years old, respectively)[22]. As TB is an airborne disease, the risk of becoming infected is associated

with the probability of coming into contact with an individual with infectious TB and the intimacy of that contact. Among contacts of individuals with infectious TB, the immunologic response to specific mycobacterial antigens increased with the spatial proximity of the subject to the individual with TB within the household. This suggests that rather than the proportion of people living in per room, it is the increased occurrence and the intimacy of contact with the individual with TB that determine the transmission of infection TB[42].

This study shows that household contact management is very important to avert TB transmission, but it is important to know that a person who is exposed to TB bacteria is not able to spread the bacteria to other people right away. Only people with active TB disease can spread TB bacteria to others. Before a person would be able to spread TB to others, he/she would have to breathe in TB bacteria and become infected[44]. In 2019, as many as 3950 child tuberculosis death could have been averted by household contact management, at a global aggregate cost-effectiveness of US \$1208 per disability-adjusted life-year averted[45].

The major strength of this analysis is that it used data from a national public health survey. This implies that it can describe the prevalence of the disease nationally with a large sample, but there are also limitations. As a national health survey with a cross-sectional method, diseases were evaluated based on interview statements using a structured questionnaire, not based on the result of laboratory measurements.

In conclusion, *M. tuberculosis* infection in children is higher in toddlers compared with other age groups in children. Contact with family who has TB is related with TB infection among children in Indonesia. Therefore, screening the household for contact with TB patients is a preventive treatment for children.

#### Conflict of interest statement

We declare that we have no conflict of interest.

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## Authors' contributions

MAN developed the conception or design of the work, data collection, data analysis and interpretation, drafting the article, critical revision of the article, final approval of the version to be published. ADL, HA, G, KT and S developed the critical revision of the article, final approval of the version to be published. IKW, V, KT, AN, O, AN developed the data analysis and interpretation, final approval of the version to be published.

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