

# Epidemiology of latent tuberculosis infection in Japan-born and foreign-born children in Japan

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**Objective:** This study aims to compare the epidemiology of notifications of latent tuberculosis infection (LTBI) among Japan-born and foreign-born children in Japan between 2010 and 2020, and to assess the language used during LTBI case interviews with parents or caregivers of foreign-born children with LTBI during 2019.

**Methods:** Our study consisted of two parts: (1) an analysis of national data from the Japan Tuberculosis Surveillance (JTBS) system on the epidemiology of LTBI among Japan-born and foreign-born children in Japan, and (2) a survey of staff at public health centres that had registered at least one foreign-born child aged  $\leq 14$  years with LTBI. Data were extracted from the JTBS system for all children aged  $\leq 14$  years who were newly notified as having LTBI between 2010 and 2020, and analysed to determine trends, characteristics and treatment outcomes. Staff at relevant public health centres completed a self-administered survey.

**Results:** A total of 7160 Japan-born and 320 foreign-born children were notified as having LTBI between 2010 and 2020. Compared with Japan-born children, foreign-born children notified as having LTBI were more likely to be older, have their mother or sibling as their source of infection and have LTBI detected via a routine school health check. At case interviews, the use of language interpretation services was limited, even when both parents were non-Japanese. No interview was directly conducted with children themselves, not even with school-aged children.

**Discussion:** Foreign-born children and their parents may be unfamiliar with the system of testing for TB infection and the diagnosis of LTBI in Japan in school settings. Public health centres are required to provide education to patients and their families and care that takes into account cultural and linguistic differences. However, the provision of language support during case interviews may need strengthening.

Japan has a low burden of tuberculosis (TB), with 11 519 cases newly notified in 2021, for a rate of 9.2/100 000 population.<sup>1</sup> Although both the number of and the notification rate for TB cases have been steadily declining, the burden of TB among foreign-born persons has been increasing.<sup>1</sup> In 2021, the proportion of foreign-born persons among total TB cases was 11.8%; however, this proportion was 68.4% among those aged 15–24 years and 67.1% among those aged 25–34 years. Approximately 80% of cases of TB among foreign-born people in Japan occur in people from six Asian countries: China, Indonesia, Myanmar, Nepal, the Philippines and Viet Nam. Slightly more than one third are notified as having TB within 2 years of entering Japan.<sup>1</sup>

Latent tuberculosis infection (LTBI) is also notifiable in Japan, and as with active TB, once notified, its treatment is publicly funded and patients receive adherence support from public health centres (PHCs), which are responsible for registering and managing treatment support for persons diagnosed with TB and LTBI. The epidemiology of LTBI follows that of active TB, whereby the proportion of foreign-born persons notified with LTBI has continued to increase.<sup>2</sup> As most cases of LTBI among foreign-born persons are diagnosed among those aged 15–34 years, more attention has been paid to providing care and treatment for adults.<sup>3,4</sup> However, a consistent number of LTBI cases have been diagnosed among foreign-born children in Japan. Patient-centred care and treatment for children with LTBI involve not only children

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Published: 23 November 2023

doi: 10.5365/wpsar.2023.14.4.1008

themselves but also their parents or caregivers. However, little is known about the treatment or support provided to foreign-born children with LTBI in Japan.

The objectives of our study were to compare the epidemiology of LTBI notifications among foreign-born and Japan-born children in Japan between 2010 and 2020, and to assess the language used during LTBI case interviews with parents or caregivers of foreign-born children with LTBI during 2019.

## METHODS

Our study consisted of two parts: (1) an analysis of national data from the Japan Tuberculosis Surveillance (JTBS) system about the epidemiology of LTBI among Japan-born and foreign-born children in Japan, and (2) a survey of staff at PHCs in Japan that had registered at least one foreign-born child aged  $\leq 14$  years with LTBI.

### Analysis of notification data

LTBI has been notifiable in Japan since 2007. In 2017, the JTBS system underwent several major revisions, one of which enabled cohort analysis for all types of TB and LTBI, which was previously possible only for pulmonary TB.

Data were extracted from the JTBS system for all children aged  $\leq 14$  years who were newly notified with LTBI between 2010 and 2020. Treatment outcomes were extracted for those notified between 2016 and 2019. The period 2016–2019 was chosen for cohort analysis since treatment outcomes for LTBI became available only from 2016. Trends and characteristics were summarized descriptively using numbers and proportions. Treatment outcomes included “treatment success”, “died”, “treatment failed”, “lost to follow up”, “transferred out”, “still in treatment” and “unknown”. Appropriate variables were compared between foreign-born children and Japan-born children using the  $\chi^2$  test with Bonferroni corrections.

### Survey of public health centres

All PHCs that had registered at least one foreign-born child aged  $\leq 14$  years with LTBI during 2019 were identified from the JTBS system. A self-administered survey was sent by email to TB personnel at each of these

PHCs. The survey consisted of questions about the basic demographics of the child (or children), parents or caregivers, and the language used during the case interview with the parents or caregivers. Numerical and categorical variables were entered into Excel spreadsheets and analysed descriptively. R version 4.2.1 (R Core Team, Vienna, Austria) was used for all statistical analyses.

## RESULTS

### Analysis of notification data

#### *Age and sex*

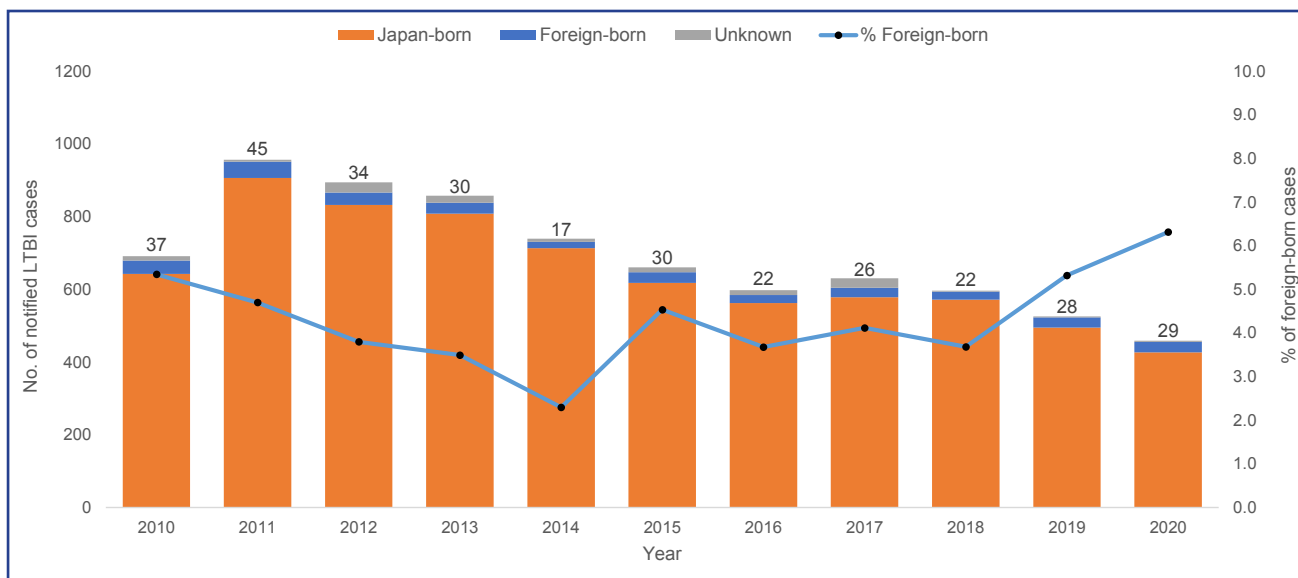
There were 7160 Japan-born and 320 foreign-born children notified with LTBI in Japan between 2010 and 2020. During this time, the annual number of case notifications in Japan declined, while the proportion of foreign-born children among all notified cases in children declined until 2014 and then increased (**Fig. 1**). In 2020, 29 cases of LTBI were notified among foreign-born children, which was 6.3% of all LTBI cases in children.

For Japan-born children, 37.1% (2663/7160) of notifications were among those aged  $< 1$  year, with the number per year declining with age (data not shown). For foreign-born children, 70% (224/320) of the notifications were for children aged 5–14 years (**Fig. 2**). The average age of foreign-born children notified with LTBI was 7.3 years (standard deviation [SD]:  $\pm 4.4$  years), while for Japan-born children it was 3.8 years (SD:  $\pm 4.4$  years) (data not shown).

#### *Country of birth and year of entry to Japan for foreign-born children*

The distribution of foreign-born children notified with LTBI by country of birth was 44.1% (141/320) from the Philippines, 12.2% ( $n = 39$ ) from China and 6.0% ( $n = 19$ ) from Viet Nam. The year of entry into Japan was recorded for 157 of the 320 foreign-born children notified with LTBI, and of these children, 25.5% ( $n = 40$ ) were diagnosed in the same year as their arrival, 26.8% ( $n = 42$ ) were diagnosed 1 year after arrival, 28.0% ( $n = 44$ ) were diagnosed 2–4 years after arrival and 19.8% ( $n = 31$ ) were diagnosed 5 years after arrival (data not shown).

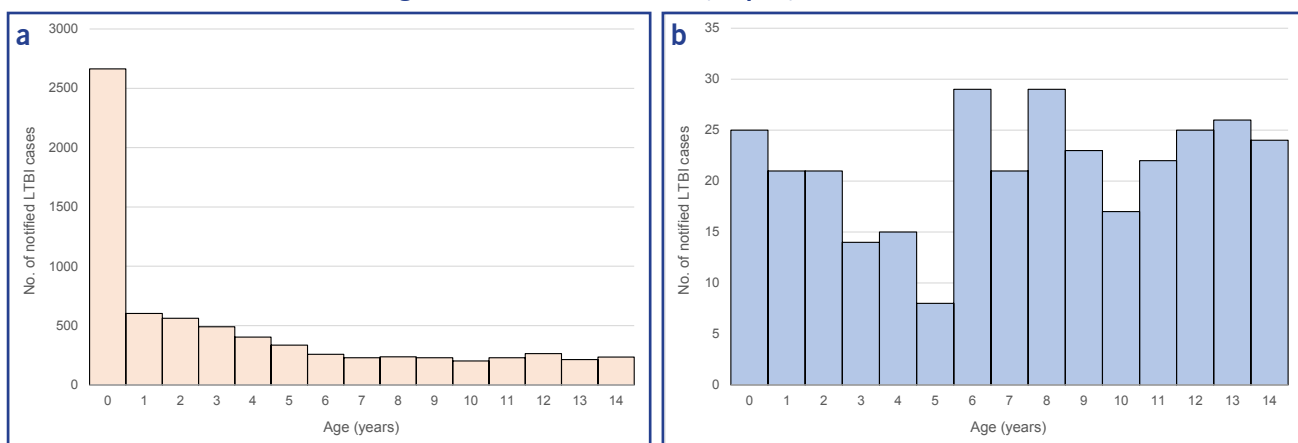
**Fig. 1. Number of new notifications of latent tuberculosis infection in children, by status as Japan-born or foreign-born and year, Japan, 2010–2020**



LTBI: latent tuberculosis infection.

Numbers above the columns indicate the number of newly notified LTBI cases among foreign-born children (dark blue).

**Fig. 2. Age distribution of children notified with latent tuberculosis infection among (a) Japan-born children ( $n = 7160$ ) and (b) foreign-born children ( $n = 320$ ), Japan, 2010–2020**



LTBI: latent tuberculosis infection.

*Mode of detection and source of infection*

The difference in distribution by mode of detection was statistically significant between Japan-born and foreign-born children notified with LTBI (Table 1;  $P < 0.001$ ). For both Japan-born and foreign-born children, the majority of LTBI cases notified were contacts of patients with active TB in the same household. A higher proportion of foreign-born cases notified with LTBI were detected through routine school health check-ups

compared with Japan-born case notifications (20.3% vs 0.5%,  $P < 0.001$ ), and there were higher proportions of Japan-born cases diagnosed during other contact investigations and in clinical settings compared with foreign-born cases notified (19.4% vs 10.9%,  $P = 0.002$  for other contact investigations; 14.0% vs 8.1%,  $P = 0.004$  for clinical settings) (Table 1).

The reported source of infection was available for 40.6% (2909/7160) of Japan-born and 34.1%

(109/320) of foreign-born LTBI notifications in children, and the difference in distribution by source of infection between the two groups was statistically significant (**Table 1**;  $P < 0.001$ ). The proportion of notifications with grandparents as the source of infection was higher for Japan-born patients (12.2% vs 5.3%,  $P = 0.002$ ), while the proportions of notifications with mothers or siblings as the source of infection were higher for foreign-born patients (14.7% vs 9.4%,  $P < 0.001$  for mothers; 3.4% vs 0.4%,  $P < 0.001$  for siblings) (**Table 1**).

### Treatment outcomes

Data on treatment outcomes between 2016 and 2019 were available for 2187 Japan-born and 99 foreign-born cases. Of these, 2162 Japan-born and 98 foreign-born cases had started LTBI treatment. The difference in treatment outcomes between the Japan-born and foreign-born cases was not statistically significant ( $P = 0.979$ ), with 91.6% (1980/2162) of Japan-born and 89.8% (88/98) of foreign-born cases completing their treatment (**Table 2**).

### Survey of public health centre staff

In 2019, 27 foreign-born children were notified with LTBI from 21 PHCs. A questionnaire survey was sent to these PHCs, of which 16 responded about 23 children. For all notifications, face-to-face case interviews were conducted upon registration by public health nurses with parents or caregivers; none of the interviews were conducted with the children themselves.

**Table 3** summarizes the nationalities of parents or caregivers (as a foreign national or Japanese national) and the language used for the interview. Among the 10 children who had one foreign-born parent, the interview was conducted with the Japanese parent for four cases, with the non-Japanese parent for four cases and with Japanese-speaking relatives for two cases. Interviews with foreign-born parents were conducted in Japanese without an interpretation service for three cases and in Tagalog for one case (**Table 3**).

Among the 12 children whose parents were both foreign nationals, the interview was conducted in Japanese for seven cases. No interpretation assistance was provided, except for one case in which the public health nurse used a mobile translation application. An

informational leaflet was used during the interview for one case, and the leaflet was in Japanese (**Table 3**). For three children, the interview was conducted in the parents' native language with the assistance of a friend or acquaintance, none of whom were professional medical interpreters. No translation apps or other tools were used. For the remaining two children, the language of the interview was not reported.

The final case had two Japanese parents and their interview was conducted in Japanese.

## DISCUSSION

Our study is the first to explore the characteristics of foreign-born children notified with LTBI in Japan. Compared with Japan-born children, foreign-born children notified as having LTBI were more likely to be older, have their mother or sibling as their source of infection and have LTBI detected via a routine school health check. That the source of infection was a first-degree relative may be due to visa regulations, as foreign-born persons working in Japan are often permitted to bring only their spouse and child (or children) and, therefore, usually live in a nuclear family. The detection of LTBI in foreign-born children during school health checks is likely due to health workers following the manual on TB prevention in schools,<sup>5</sup> which recommends tuberculin skin testing (TST) or interferon- $\gamma$  release assay (IGRA) testing for children from countries with a high TB burden upon entry to primary school and LTBI treatment for those who test positive.

In the majority of countries where these children were born (i.e. countries with a high TB burden), routine LTBI screening is not conducted. Rather, LTBI treatment is usually offered only to children aged  $\leq 5$  years who are household contacts of active TB cases, after active TB has been ruled out, but neither TST nor IGRA are usually conducted as part of household contact investigations.<sup>6–8</sup> Therefore, it is expected that many foreign-born children and their parents in Japan are unfamiliar with the experience of being tested for and diagnosed with LTBI, and even less familiar with this in school settings. Thus, PHCs are required to provide education to patients and families and care that accounts for these differences.

Furthermore, previous studies have shown that children may face different barriers to initiating and

Table 1. **Mode of detection and possible source of infection for notifications of latent tuberculosis infection in Japan-born and foreign-born children, Japan, 2010–2020**

Characteristic	No. (%) of children				P
	Japan-born		Foreign-born		
<b>Total</b>	7160	(100.0)	320	(100.0)	
<b>Mode of detection</b>					< 0.001
Household contact investigation	3718	(51.9)	156	(48.8)	
Other contact investigation	1390	(19.4)	35	(10.9)	
School health check-up	33	(0.5)	65	(20.3)	
Other mass health check-up	125	(1.7)	4	(1.3)	
Clinical setting	1001	(14.0)	26	(8.1)	
Other or unknown	893	(12.5)	34	(10.6)	
<b>Source of infection</b>					< 0.001
Mother	671	(9.4)	47	(14.7)	
Father	516	(7.2)	18	(5.6)	
Grandparent	875	(12.2)	17	(5.3)	
Sibling	32	(0.4)	11	(3.4)	
School	212	(3.0)	3	(0.9)	
Friends (outside school)	34	(0.5)	1	(0.3)	
Hospital	81	(1.1)	0	(0.0)	
Other	488	(6.8)	12	(3.8)	
Unknown	4251	(59.4)	211	(65.9)	

Table 2. **Treatment outcomes for notifications of latent tuberculosis infection in Japan-born and foreign-born children who had started treatment, Japan, 2016–2019**

Treatment outcome	No. (%) of children		P
	Japan-born	Foreign-born	
Total <sup>a</sup>	2162 (100.0)	98 (100.0)	0.979
Completed	1980 (91.6)	88 (89.8)	
Died	1 (0.0)	0 (0.0)	
Failed	3 (0.1)	0 (0.0)	
Lost to follow-up	58 (2.7)	3 (3.1)	
Transferred out	47 (2.2)	3 (3.1)	
Still on treatment	67 (3.1)	4 (4.1)	
Unknown	6 (0.3)	0 (0.0)	

<sup>a</sup> A total of 25 Japan-born children and one foreign-born child had not started treatment at the time of analysis; they are not included in the analysis of treatment outcomes.

completing LTBI care compared with adults.<sup>9–11</sup> Some barriers are patient-related factors, such as knowledge, concerns about side-effects and the school environment, which may be important to older children.<sup>12,13</sup> However,

especially with younger children, treatment decisions are made by parents or caregivers, and their knowledge and perceptions regarding TB infection,<sup>9</sup> the adverse effects of medication<sup>14,15</sup> and medical contraindications to treatment,<sup>16,17</sup> personal health beliefs<sup>13,18,19</sup> and relationship with their children<sup>20</sup> have been shown to play important roles in treatment completion. In studies from lower-income countries, socioeconomic factors have also been identified as barriers to treatment completion, such as low monthly income,<sup>9</sup> high cost of transport<sup>9</sup> and conflicts with work schedules,<sup>13</sup> which all place burdens on parents or caregivers.

Our results showed that the case interviews at PHCs were largely conducted in Japanese, with limited use of language interpretation services, either in person or via an app, even when neither of the parents were Japanese nationals. Previous studies have repeatedly shown there is limited availability of medical interpretation services for foreign-born patients with<sup>21,22</sup> and without TB<sup>23,24</sup> in Japan and that language is a major barrier to accessing health care for foreign-born persons in Japan.

**Table 3. Language spoken during case interview for notifications of latent tuberculosis infection in foreign-born children, by nationality of their parents, Japan, 2019**

Nationality of parents	No.	Language of the interview		Translation app used
		Japanese	Other	
One parent is a foreign national	10	9	1	0
Both parents are foreign nationals <sup>a</sup>	12	7	3	1
Both parents are Japanese nationals	1	1	0	0
Total	23	17	6	1

<sup>a</sup> No information was provided about the language used during the interview for two of the cases.

Our study is not without limitations, and the most significant is that the study was limited to children notified with LTBI to the JTBS system. Therefore, it was unable to capture those children who, although eligible for LTBI treatment, were not notified and thus had not started treatment. The JTBS system also did not capture the total number of children tested for LTBI nor those who tested negative. A scoping review on care cascades for paediatric LTBI has identified several stages during which dropout from the cascade could occur.<sup>24</sup> In Japan, too, it is quite possible that some foreign-born children who are eligible never begin LTBI treatment. A comprehensive study to capture the care cascade for foreign-born children diagnosed with LTBI, both before travelling to and after entering Japan, is needed. Second, our survey specifically focused on the language spoken during the case interview and did not explore other issues, such as knowledge and attitudes towards and practices around LTBI between Japan-born and foreign-born children and their parents. Further studies are needed to explore these differences.

Our study indicated that foreign-born children notified with LTBI tended to be older, have their mother or sibling identified as the source of infection, and be detected via a routine school health check. The use of language interpretation services by health-care providers and the parents or caregivers of children diagnosed with LTBI in 2019 was limited. This may lead to poorer communication, knowledge and understanding about TB infection and the necessity for preventive treatment, as well as a lack of trust. Action is needed to address long-standing issues around language barriers for foreign-born persons, both children and adults, in Japan.

### *Acknowledgements*

The authors acknowledge all public health centre staff who kindly gave their time to participate in the survey.

### *Conflicts of interest*

The authors have no conflicts of interest to declare.

### *Ethics statement*

This study was approved by the Institutional Review Board of the Research Institute of Tuberculosis, Japan (reference no. RIT/IRB 2020-18).

### *Funding*

This research was partially supported by a Grant-in-Aid for Scientific Research from the Japan Society for the Promotion of Science (grant no. 20K10491).

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