Pediatric Tuberculosis at Beijing Children's Hospital: 2002–2010

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KEY WORDS
childhood, China, epidemiology, hospital, risk factors, tuberculosis

ABBREVIATIONS
AFB—acid-fast bacilli
BCG—bacille Calmette-Guérin
CI—confidence interval
DTB—disseminated tuberculosis
EPTB—extrapulmonary tuberculosis
INH—isoniazid
MTB—*Mycobacterium tuberculosis*
OR—odds ratio
PPD—purified protein derivative
PTB—pulmonary tuberculosis
RFP—rifampicin
TBM—tuberculous meningitis

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WHAT'S KNOWN ON THIS SUBJECT: Pediatric tuberculosis is significant for public health professionals because it is an indicator of the recent transmission of tuberculosis in the community. Data on incidence and clinical features of pediatric tuberculosis from China are scarce.

WHAT THIS STUDY ADDS: We conducted this study to describe the patient characteristics, clinical–epidemiological profile, and treatment outcomes for pediatric tuberculosis in a referral hospital setting in China.

abstract

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OBJECTIVE: Our aim was to describe the patient characteristics, clinical–epidemiological profile, and treatment outcome of childhood tuberculosis (TB).

METHODS: A retrospective, descriptive study was undertaken of 1212 children aged 0 to 18 years admitted to Beijing Children's Hospital for the treatment of TB from January 2002 to December 2010. Statistical significance of category variables was evaluated by using Fisher's exact test.

RESULTS: Fifty-four percent of patients had extrapulmonary tuberculosis (EPTB), 38.8% had tuberculous meningitis, and 31.3% had disseminated TB. The last 2 types were defined as severe TB. Most patients with TB (81.6%) were cured or completed treatment. There were more patients aged <5 years and from rural areas with EPTB than with pulmonary tuberculosis. More severe cases of TB were found in patients aged <1 year than other less severe types of TB. Patients with no bacille Calmette-Guérin vaccination and a contact history at home had a significantly risk of contracting severe TB. Children aged <1 year and those with severe TB were more likely to have poor treatment outcomes (failed to improve or died). Among those with EPTB, only 61.3% and 61.1% had positive results on the purified protein derivative tuberculin skin test and chest radiograph, respectively.

CONCLUSIONS: In this referral hospital setting, more pediatric EPTB and severe TB patients were found among children aged <1 year. Age <1 year and having severe TB were risk factors for treatment failure. Thus, prevention and health care in pediatric TB should focus on both EPTB and severe TB. *Pediatrics* 2012;130:e1433–e1440

Tuberculosis (TB) among children is significant for public health professionals because it is an indicator of the recent transmission of TB in the community.[1] However, national TB control programs emphasize sputum smear–positive adult TB cases because they are highly infectious. Data on incidence and clinical features of childhood TB are scarce.[2,3]

In China, the fourth nationwide random survey of the epidemiology of TB was conducted in 2000.[4] The active pulmonary TB (PTB) prevalence rate in children aged 0 to 14 years was 91.8 per 100 000, the bacteriologic-positive PTB prevalence rate was 12.3 per 100 000, and the smear-positive PTB prevalence rate was 6.7 per 100 000. The TB prevalence rate in children has not substantially decreased from 1979 to 2000. However, studies on the epidemiology, clinical profile, and treatment outcomes of childhood TB from developing countries are lacking, and reports from elsewhere describe populations with distinctly different epidemiological profiles, such as 1 with a high incidence of HIV-coinfected children,[5] which is rare in China.

This study was performed in a regional referral hospital for TB in China to describe the patient characteristics, clinical profile, and treatment outcomes of pediatric TB.

METHODS

Study Population

This study was conducted between January 2002 and December 2010 at Beijing Children's Hospital, the largest children's hospital in China. The wards of the Pediatric Internal Medicine Department had 22 642 admissions in 2002 and 42 380 admissions in 2010. All children diagnosed with TB and admitted to the TB wards of the Pediatric Internal Medicine Department were included in this retrospective study. Capital Medical University provided ethical clearance, and the medical director of Beijing Children's Hospital provided permission to access medical records.

Criteria for Pediatric TB Diagnosis, Treatment, and Classification

Diagnosis was performed according to the guidelines of the Chinese Medical Association[6]: (1) clinical presentation (symptoms or signs); (2) chest radiography and computed tomography scan; (3) contact history (family, close contact); (4) purified protein derivative (PPD) tuberculin skin test (using 5 TU); (5) bacteriologic examination (including examination of sputum, tuberculous pleural effusion, bronchoalveolar lavage, gastric aspirates, cerebrospinal fluid, and peritoneal fluid); (6) bronchoscopy; and (7) biopsy if necessary. The gold standard diagnosis of TB is made when *Mycobacterium tuberculosis* (MTB) is isolated.

The basic treatment and standard anti-TB regimens for children were provided according to the guidelines of the Chinese Medical Association.[6] Treatment of most forms of PTB and extrapulmonary TB (EPTB) consists of a 6-month, short-course chemotherapy regimen with 4 drugs (isoniazid [INH], rifampicin [RFP], ethambutol, and pyrazinamide) in the initial 2-month intensive phase, followed by 2 drugs (INH and RFP) in the 4-month continuation phase.

Definitions

PTB[7–9]: Patients with exclusively intrathoracic involvement (ie, confined to the lung parenchyma, pleura, and intrathoracic lymph nodes) were considered to have PTB.

EPTB[7–9]: Patients with pulmonary involvement who also had extension of the disease to organs or tissues outside the thorax were classified as having EPTB.

Disseminated TB: Patients with ≥2 noncontiguous sites with TB lesions were considered to have disseminated TB (DTB).

Severe TB[10]: Severe TB included those patients with DTB or tuberculosis meningitis (TBM).

Bacille Calmette-Guérin vaccinated[11]: Previous bacille Calmette-Guérin (BCG) vaccination was determined by either the presence of a scar on the left upper arm or record of BCG vaccination.

Non–BCG vaccinated: Patients were considered to not be BCG vaccinated if there was no scar on the upper arm or no record of BCG vaccination.

Close contact[12]: A close contact was defined as living in the same household or in frequent contact with a source case (eg, caregiver) with sputum smear–positive TB. If the source cases were sputum smear–negative but culture-positive and still infectious, those cases were still considered as the source of close contact in our study.

Treatment outcomes of childhood TB[13]: Treatment outcome was reported as either cured, treatment completed (no culture results available), treatment failed, defaulted, or died.

Cured[13]: A initial sputum smear–positive TB patient who completed treatment and had negative sputum smears on 2 occasions, 1 of which was at the end of treatment, was considered cured.

Treatment completed[13]: Patients were considered to have completed treatment if they were 1 of the following: a sputum smear–positive TB patient who completed treatment, with negative smears at the end of the intensive phase and had not become smear-positive at the end of treatment; a sputum smear–negative TB patient who received a full course of treatment and had not become smear-positive during or at the end of treatment; or an EPTB patient who received a full course of

treatment and had not become smear-positive during or at the end of treatment.

Death[13]: Patient who died during the course of treatment, regardless of cause.

Failure[13]: Any TB patient who was smear-positive at ≥5 months after starting treatment. Failure also included patients treated with a category III regimen (INH, RFP, and pyrazinamide thrice weekly for a 2-month intensive-phase; INH and RFP thrice weekly for a 4-month phase) but who became smear-positive during treatment.

Defaulted[13]: A patient who had not taken anti-TB drugs for ≥2 consecutive months after starting treatment was considered to have defaulted.

Transferred out[13]: A patient was considered to have transferred out if he or she transferred to another TB unit or other district, and the treatment outcome was not known.

Statistical Analyses

SPSS version 13.0 (SPSS Inc, Chicago, IL) was used for statistical analyses. All statistical hypothesis tests were 2-sided, and *P* values <.05 were considered statistically significant. Categorical variables were compared by using Fisher's exact test. Unadjusted and adjusted odds ratios (ORs) were calculated by using univariable and multivariable logistic regression analyses. Variables with significant impact on the risk of poor treatment outcome (failed or died) in univariable analysis were entered stepwise into the multivariable model by using the forward conditional method.

RESULTS

Demographic and Clinical Data

Between January 2002 and December 2010, a total of 1212 children hospitalized with TB were enrolled in the study; 63.2% (*n* = 766) were male (Table 1). There was no significant difference in gender distribution by age, but there were more males in all age groups (Table 2). Age was given as median and interquartile range and classified into subgroups (<1, 1–4, 5–12, and 13–18 years), as suggested by the World Health Organization.[2,14] The median age of patients was 5.5 years (interquartile range: 1.5–11 years), and the age range was 2 months to 18 years. More patients (54.0%) were classified as having EPTB than PTB. Of those with EPTB, the most common diagnosis was TBM (38.8%) followed by DTB (31.3%). Both types were defined as severe TB. Of the 24% of patients with TB who had not received the BCG vaccine, 25% did not visit our hospital until ≥60 days after the onset of TB symptoms (Table 1). Overall, 975 (80.4%) completed treatment, and 14 (1.2%) were cured. However, 173 patients (14.3%) failed to improve with treatment, and 5 (0.4%) died. The failure rate (failed treatment plus died) was 15.3% (178 of 1167), and the treatment success rate (cured plus treatment completed) was 84.7% (989 of 1167).

TB Proportion in the Hospital

During this 9-year period, the annual number of TB patients increased from 121 in 2002 to 166 in 2007, then decreased slightly to 144 in 2010. However, the proportion of pediatric patients with TB decreased slightly over time, from 0.53% in 2002 to 0.34% in 2010 (Fig 1).

Distribution of EPTB Types by Age

The distribution of types of EPTB differed by age (Fig 2). In the youngest patients (aged <1 year), DTB was the most frequent type of EPTB (67.4%), followed by TBM (20.6%) and tuberculous lymphadenitis (7.8%). For older children, TBM was the most frequent type (44.7% in those aged 1–4 years, 44.8% in those aged 5–12 years, and 37.3% in those aged 13–18 years). In addition, the proportion of abdominal TB increased gradually with age (2.8%, 5.3%, 20.9%, and 34.3%, respectively, in the 4 age groups).

PTB Versus EPTB

Age was significantly associated with TB type (*P* < .001); 67.1% and 59.6% of patients <1 and 1 to 4 years old had

TABLE 1 Characteristics of Pediatric Patients With TB (*N* = 1212)

Characteristic	*N* (%)
Age group, y	
<1	210 (17.3)
1–4	349 (28.8)
5–12	479 (39.5)
13–18	174 (14.4)
Gender	
Female	446 (36.8)
Male	766 (63.2)
Location	
Rural	819 (67.6)
City	262 (21.6)
County	131 (10.8)
BCG vaccinated	
Yes	886 (76.0)
No	280 (24.0)
Time from onset of symptoms to hospital visit, d	
0–30	661 (54.7)
31–60	235 (19.4)
61–90	110 (9.1)
>90	203 (16.8)
TB type	
PTB	557 (46.0)
EPTB	655 (54.0)
TBM	254/655 (38.8)
DTB	205/655 (31.3)
Abdominal TB	88/655 (13.4)
Bone/joint TB	61/655 (9.3)
TBL	32/655 (4.9)
Other	15/655 (1.2)
Contact history at home	
Yes	364 (31.0)
No	809 (69.0)
Severity of TB[a]	
Severe	459 (37.9)
Other	753 (62.1)
Treatment outcome	
Cured	14 (1.2)
Completed	975 (80.4)
Failed to improve	173 (14.3)
Died	5 (0.4)
Lost to follow-up[b]	45 (3.7)

Missing rate: BCG vaccinated, 46 (3.8%); period from onset of symptoms to care, 3 (0.2%); contact history at home, 39 (3.2%). TBL = tuberculous lymphadenitis.

[a] Severe TB: DTB and TBM; Other TB: other than severe TB.

[b] Indicates a patient whose parent refused additional therapy in the hospital; the child was discharged; and the hospital has since lost contact with the family.

TABLE 2 TB Distribution According to Age and Gender

Age Group	Total *N*	Female	Male
<1 y	210	79 (37.6%)	131 (62.4%)
1–4 y	349	123 (35.2%)	226 (64.8%)
5–12 y	479	171 (35.7%)	308 (64.3%)
13–18 y	174	73 (42.0%)	101 (58.0%)

Data are presented by count and horizontal percentage; $P = .448$, 5 × 2 comparison of male and female patients in different age groups.

EPTB, but only 32.9% and 40.4% <1 and 1 to 4 years old had PTB (Table 3). In contrast, more patients had PTB than EPTB in the older groups (5–12 and 13–18 years old). Location of residence was also associated with TB type ($P = .023$). Children from rural areas had more EPTB (56.7%) than PTB (43.3%), but children from county (township) areas had more PTB (54.2%) than EPTB (42.5%).

Severe TB Versus Other TB

Age was significantly associated with severity ($P < .001$); 59.0% of patients aged <1 year had severe TB, but only 41.0% of patients aged <1 year had other types of TB (Table 3). In contrast, the percentage of "severe TB" patients was less than "other TB" patients in other older groups (43.8% vs 56.2% in 1–4 y, 30.1% vs 69.9% in 5–12 y, and 21.8% vs 8.2% in 13–18y). Location of residence was also associated with severity ($P < .001$). Less than 30% of children from city and county (township) areas had severe TB. BCG vaccination was also associated with severity ($P < .001$). For those patients with no BCG vaccination, 48.6% of patients had severe TB, which was significantly higher than the 34.3% of severe TB among those children with a BCG vaccination. For the children who did not come for a hospital visit until 30 days after the onset of symptoms, more patients (~60%) suffered from other types of TB than the patients with severe TB ($P < .001$), suggesting that patients with less severe TB might delay the time to visit the hospital. Finally, contact history was also associated with severity ($P = .003$). For the children without a contact history at home, only 35.2% of patients had severe TB, but 44.5% of patients had severe TB among the children with contact history at home, suggesting that children with contact history at home had a higher chance of contracting severe TB (Table 3).

Risk Factors for Poor Treatment Outcome

Age, TB type (EPTB versus PTB), and severity (severe TB versus other TB) were significantly associated with treatment outcome. For unadjusted odds ratios (ORs), estimated by using a univariable logistic regression analysis, children <1 year old were more likely to have a poor outcome (failed to improve with treatment or died) than those aged 13 to 18 years ($P = .011$), with an unadjusted OR of 2.06 (95% confidence interval [CI]: 1.18–3.57]). Children with EPTB were more likely to have a poor outcome than those with PTB, with an unadjusted OR of 1.50 (95% CI: 1.08–2.10). Children with severe TB were more likely to have a poor outcome than those with another type of TB, with an unadjusted OR of 1.71 (95% CI: 1.24–2.36).

Multivariable logistic regression (Table 4), which controlled for disease severity, indicated that children aged <1 year were more likely to have a poor outcome (failed to improve with treatment or died) than patients who were 13 to 18 years old ($P = .05$), with an adjusted OR of 1.76 (95% CI: 0.9989–3.11). In addition, children with severe TB were more likely to have a poor outcome (failed to improve with treatment or died) than those with other TB types ($P = .016$), with an adjusted OR of 1.50 (95% CI: 1.08–2.10).

Relative Results of Diagnostic Tests Between PTB and EPTB

A total of 811 children (70.2%) had positive results on the PPD tuberculin skin test, and 957 children (79.0%) had positive chest radiography results. Significantly fewer EPTB patients than PTB patients had positive PPD results (61.3% vs 80.1%; $P < .001$). In addition, 56 children (5.9%) and 136 children (14.4%) had positive results on the acid-fast bacilli (AFB) stain and MTB culture results, respectively. There was no significant difference between EPTB and PTB patients in the percentage of positive AFB stain results (7.0% vs 4.7%) and MTB culture results (13.2% vs 15.7%) (Table 5).

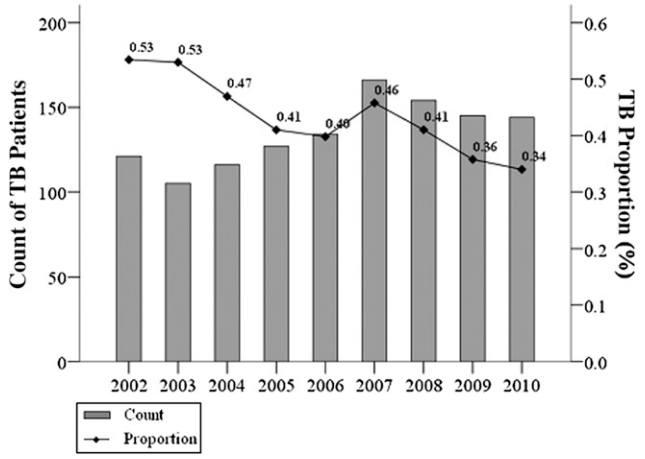
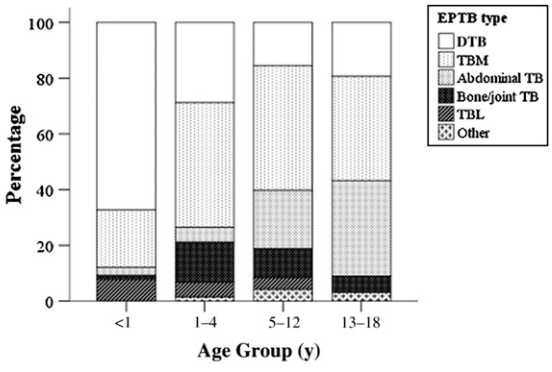


FIGURE 1
Number and proportion of pediatric patients with TB at Beijing Children's Hospital.

DISCUSSION

In our analysis of the medical records of 1212 patients with TB, the total number of



	<1	1–4	5–12	13–18
DTB	95 (67.4%)	60 (28.8%)*	37 (15.5%)*	13 (19.4%)*
TBM	29 (20.6%)	93 (44.7%)*	107 (44.8%)*	25 (37.3%)
Abdominal TB	4 (2.8%)	11 (5.3%)	50 (20.9%)***	23 (34.3%)***
Bone/joint TB	2 (1.4%)	30 (14.4%)*	25 (10.5%)*	4 (6.0%)
TBL	11 (7.8%)	11 (5.3%)	10 (4.2%)	0 (0.0%)
Other	0 (0.0%)	3 (1.4%)	10 (4.2%)	2 (3.0%)

FIGURE 2

Patients with EPTB were stratified according to age into those aged <1 year, 1 to 4 years, 5 to 12 years, and 13 to 18 years. TBL = tuberculous lymphadenitis; other = tuberculous pericarditis, renal TB, or tuberculosis cutis. *Indicates a significant difference in the proportion compared with those aged <1 year. **Indicates a significant difference in the proportion compared with those aged 1 to 4 years.

childhood TB patients increased from 2002 to 2007, then fell slightly in recent years, although it was higher in 2010 than in 2002 (Fig 1). This increase may be attributed to an increased prevalence of TB, better TB diagnosis, or greater parental attention to TB. However, over the same time period, the percentage of TB patients who were children declined (from 0.53% in 2002 to 0.34% in 2010). This decrease in the proportion of pediatric TB patients was mainly due to the increase in the total number of admitted patients. There were more males in all age groups, which can be partially explained by the higher birth rate of males in China.[15] In the patients described here, the treatment success rate (cured plus treatment completed) was 81.6%. This finding is only slightly lower than a previous report,[4] in which the cure rates for new cases and retreatment patients were 95.1% and 89.6%, respectively.

Distribution of types of TB in children was similar across 2002–2010. Pulmonary parenchymal disease and intrathoracic adenopathy are the most common clinical manifestations of pediatric TB, accounting for 60% to 80% of cases.[16,17] However, our data showed that PTB and EPTB accounted for 46.0% and 54.0% of all TB in children, respectively. The

TABLE 3 Comparison of Patient Characteristics According to TB Type and Severity

Characteristic	*N*	PTB (*n* = 557)	EPTB (*n* = 655)	*P* Value	Severe TB[a] (*n* = 459)	Other TB[b] (*n* = 753)	*P* Value
Age, y							
<1	210	69 (32.9%)	141 (67.1%)	<.001*	124 (59.0%)	86 (41.0%)	<.001*
1–4	349	141 (40.4%)	208 (59.6%)		153 (43.8%)	196 (56.2%)	
5–12	479	240 (50.1%)	239 (49.9%)		144 (30.1%)	335 (69.9%)	
13–18	174	107 (61.5%)	67 (38.5%)		38 (21.8%)	136 (78.2%)	
Gender							
Female	446	189 (42.4%)	257 (57.6%)	.064	182 (40.8%)	264 (59.2%)	.111
Male	766	368 (48.0%)	398 (52.0%)		277 (36.2%)	489 (63.8%)	
Location							
Rural	819	355 (43.3%)	464 (56.7%)	.023*	343 (41.9%)	476 (58.1%)	<.001*
City	262	131 (50.0%)	131 (50.0%)		77 (29.4%)	185 (70.6%)	
County	131	71 (54.2%)	60 (45.8%)		39 (29.8%)	92 (70.2%)	
BCG vaccinated							
Yes	886	423 (47.7%)	463 (52.3%)	.054	304 (34.3%)	582 (65.7%)	<.001*
No	280	115 (41.1%)	165 (58.9%)		136 (48.6%)	144 (51.4%)	
Time from onset of symptoms to hospital visit, d							
0–30	661	313 (47.4%)	348 (52.6%)	.632	276 (41.8%)	385 (58.2%)	<.001*
31–60	235	105 (44.7%)	130 (55.3%)		92 (39.1%)	143 (60.9%)	
61–90	110	50 (45.5%)	60 (54.5%)		41 (37.3%)	69 (62.7%)	
>90	203	86 (42.4%)	117 (57.6%)		50 (24.6%)	153 (75.4%)	
Contact history at home							
Yes	364	161 (44.2%)	203 (55.8%)	.486	162 (44.5%)	202 (55.5%)	.003*
No	809	376 (46.5%)	433 (53.5%)		285 (35.2%)	524 (64.8%)	

Data are presented by count and horizontal percentage. County refers to a township and nearby area and rural refers to countryside consisting predominantly of farmlands or mountain areas.

[a] Severe TB: DTB and TBM; Other TB: other than severe TB.

* Indicates a significant association according to Fisher's exact test.

TABLE 4 Association of Patient Characteristics With Treatment Outcome

Characteristic	*N*	Treatment Outcome		Unadjusted OR (95% CI)	*P* Value	Adjusted OR (95% CI)	*P* Value
		Cured/Completed (*n* = 989)	Failed/Died (*n* = 178)				
Age, y							
<1	203	155 (76.4%)	48 (23.6%)	2.06 (1.18–3.57)	.011*	1.76 (0.9989–3.11)	.050
1–4	334	279 (83.5%)	55 (16.5%)	1.31 (0.77–2.23)	.324	1.19 (0.69–2.05)	.523
5–12	462	409 (88.5%)	53 (11.5%)	0.86 (0.51–1.46)	.578	0.83 (0.48–1.41)	.484
13–18	168	146 (86.9%)	22 (13.1%)	Reference		Reference	
Gender							
Male	746	642 (86.1%)	104 (13.9%)	0.76 (0.55–1.05)	.098		
Female	421	347 (82.4%)	74 (17.6%)	Reference			
Location							
Rural	787	659 (83.7%)	128 (16.3%)	Reference			
City	255	224 (87.8%)	31 (12.2%)	0.71 (0.47–1.09)	.114		
County	125	106 (84.8%)	19 (15.2%)	0.92 (0.55–1.56)	.764		
BCG vaccinated							
Yes	852	721 (84.6%)	131 (15.4%)	1.02 (0.70–1.49)	.922		
No	271	230 (84.9%)	41 (15.1%)	Reference			
Time from onset of symptoms to hospital visit, d							
0–30	639	549 (85.9%)	90 (14.1%)	Reference			
31–60	228	197 (86.4%)	31 (13.6%)	0.96 (0.62–1.49)	.855		
61–90	108	85 (78.7%)	23 (21.3%)	1.65 (0.99–2.75)	.055		
>90	191	157 (82.2%)	34 (17.8%)	1.32 (0.86–2.04)	.207		
TB type							
EPTB	630	519 (82.4%)	111 (17.6%)	1.50 (1.08–2.08)	.015*		
PTB	537	470 (87.5%)	67 (12.5%)	Reference			
Severity of TB[a]							
Severe	448	360 (80.4%)	88 (19.6%)	1.71 (1.24–2.36)	.001*	1.50 (1.08–2.10)	.016*
Other	719	629 (87.5%)	90 (12.5%)	Reference		Reference	

Data are presented by count and horizontal percentage.

* Indicates a significant impact on the risk of failed/died by using logistic regression analysis. Unadjusted OR indicates the unadjusted OR estimated by using univariable logistic regression analyses. Adjusted OR indicates the OR estimated by using multivariable logistic regression analyses.

[a] Severe TB: DTB and TBM; Other TB: other than severe TB.

results were similar to those of other studies, such as in Uganda[18] and Nepal,[19] in which >50% of children hospitalized with TB had EPTB. This high proportion of EPTB in children may be due to their immature immune systems: TB often progresses rapidly from infection with MTB to disease. PTB may also have been significantly underdiagnosed during this period.[20] The most common location for EPTB in our study was TBM (38.8%) followed by DTB (31.3%). In contrast, other studies[10,19] have reported that the lymph nodes are the leading presentation for patients with EPTB. The difference may lie in our study being a hospital-based series of pediatric TB patients who are likely to be more ill than those diagnosed as outpatients and may therefore have higher rates of severe TB (TBM and DTB).

The most prevalent age for pediatric TB in this study was <5 years. Children in this group accounted for 46.1% of cases, which is comparable with results from previous studies.[21–23] EPTB has previously been reported in 68.7% of children aged <5 years but in only 15% of adolescents.[23] We found similar results, with EPTB more common in younger children: 67.1% in infants (age <1 year) and 59.6% in those aged 1 to 4 years. The distribution of types of EPTB differed by age, with DTB most frequently seen in children aged <1 year (67.4%), which confirms previous observations that the highest risk of serious TB disease is in children aged <2 years.[24,25] The overwhelming bacillemia that accompanies DTB serves to increase the incidence of meningeal TB.[26] The proportion of TBM cases among children with TB aged <1 year (20.6%) was lower than that observed in the Western Cape of South Africa for the period 1985 to 1987 (51.7%).[27] Reasons for this difference may lie in the diagnostic delay in the community hospital setting. The difficulty of diagnosing TBM in young children usually causes a delay in diagnosis.[28]

BCG is the most widely used TB vaccine worldwide and is given to infants at birth to prevent TB.[29] In our study, the proportion of EPTB in our BCG-vaccinated group was slightly lower than in the non–BCG vaccinated group (52.3% vs 58.9%), but the difference was not statistically significant. However, for those patients with no BCG vaccination, 48.6% of patients had severe TB, which was significantly higher than the 34.3% of severe TB among those

TABLE 5 Results of Diagnostic Tests for Patients With PTB and EPTB

Diagnostic Test	PTB (n = 557)	EPTB (n = 655)	P Value
PPD tuberculin skin test (positive)	438/547 (80.1%)	373/608 (61.3%)	<.001*
Chest radiograph (positive)	557/557 (100.0%)	400/655 (61.1%)	<.001*
AFB stain (positive)[a]	21/446 (4.7%)	35/500 (7.0%)	.167
MTB culture (positive)[b]	70/446 (15.7%)	66/500 (13.2%)	.307

Data were presented by the positive number/number of patients on whom the procedure investigation was conducted and the percentage.

[a] The 56 AFB stain–positive specimens were from sputum (21 [37.5%]), gastric aspirates (19 [33.9%]), bronchoalveolar lavage (13 [23.2%]), cerebrospinal fluid (5 [8.9%]), pleural effusion (4 [7.1%]), urine (2 [3.6%]), lymph node biopsy (2 [3.6%]), skin secretion (2 [3.6%]), and peritoneal fluid (1 [1.8%]).

[b] The 136 MTB culture–positive specimens were from gastric aspirates (43 [31.6%]), bronchoalveolar lavage (37 [27.2%]), cerebrospinal fluid (34 [25.0%]), sputum (32 [23.5%]), pleural effusion (8 [5.9%]), peritoneal fluid (3 [2.2%]), skin secretion (3 [2.2%]), lymph node biopsy (2 [1.5%]), urine (1 [0.7%]), and pus (1 [0.7%]).

* Indicates a significant association with TB type by the Fisher's exact test.

children with a BCG vaccination. This finding suggests that children who had received a BCG vaccination might have less chance of contracting severe TB. Although we cannot conclude that BCG vaccination is protective based on our data alone, many previous studies have indicated that the BCG vaccine is effective in preventing DTB and TBM.[26,30–33]

In this study, we found a significantly high proportion (44.5%) of severe TB in those reporting close contact history at home but only 35.2% in those not reporting close contacts. Children who live with adults known to have active TB are at risk for developing TB. Close contact with an infectious PTB source case poses a transmission risk of 30% to 80% in infants, with a risk of 60% to 80% for sputum AFB smear-positive and 30% to 40% for smear-negative source cases.[34] Most contacts are immediate relatives (usually household members).[35]

Our study had several limitations. Our sample was drawn from a referral hospital, and such cases tend to be more severe, which might result in sampling bias. However, this hospital is the major referral hospital for childhood TB in northern China, and thus may represent the status of pediatric TB in this region. Some important clinical and demographic information was incomplete or missing from the medical records. Some factors, such as delay in diagnosis, poor compliance, incorrect diagnosis, and multidrug-resistant TB, were not included.

CONCLUSIONS

Pediatric TB cases at China's largest pediatric referral hospital indicated that EPTB was more common in children than PTB, and most pediatric EPTB patients were aged <5 years. More severe TB cases were found in those patients aged <1 year. Patients with no BCG vaccination and contact history at home might have a higher risk of contracting severe TB. Thus, prevention and health care in pediatric TB should focus on both EPTB and severe TB, and patients aged <1 year should be treated with special care.

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