

Ten-year experience of children with tuberculosis in southern Taiwan

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Background and purpose: Data on the clinical characteristics of pediatric tuberculosis (TB) are limited. This retrospective study was performed to evaluate the demographic characteristics and clinical features of pediatric TB.

Methods: The medical records of children with TB at Kaohsiung Veterans General Hospital, Kaohsiung, Taiwan, between 1992 and 2002 were analyzed for demographic and clinical characteristics, and treatment regimens.

Results: 103 children aged 0 to 14 years with probable or confirmed TB were enrolled. Ninety patients (87.4%) had pulmonary tuberculosis (PTB) and 13 (12.6%) had extrapulmonary tuberculosis (EPTB). The mean \pm standard deviation age of children with PTB and with EPTB was 6.0 ± 4.2 years and 4.5 ± 5.4 years, respectively. Household contact was the route of infection for 44.4% of patients with PTB and 7.7% of patients with EPTB. TB in children aged 0 to 4 years most commonly involved the lung (53.3%) or the extrapulmonary region (69.2%). Common symptoms of PTB were cough (81.1%) and fever (33.3%). The most frequent sites of pediatric EPTB were bone ($n = 4$) and cervical lymph nodes ($n = 4$). Tuberculin skin test (TST; ≥ 10 mm) was positive in 69.6% of children with PTB (55/79) and 37.5% of children with EPTB (3/8). Children with PTB had a lower positive acid-fast bacilli rate (40.0%) and *Mycobacterium tuberculosis* culture (27.8%). Eighty percent of patients infected through household contact had a positive TST.

Conclusion: Prolonged cough, household TB contact, and positive TST were characteristic factors for children with PTB in southern Taiwan. Young age was associated with high morbidity.

Key words: Tuberculosis; Tuberculosis pulmonary

Introduction

Tuberculosis (TB) has reached epidemic proportions in developing countries [1-3]. Since 1985, there has been an increase in the number of patients with active TB in the United States, largely among new immigrants and children younger than 15 years [2-5]. However, between 1986 and 1993 in Maryland, United States, the incidence of pediatric TB showed a downward trend [6]. The prevalence and mortality of TB in Taiwan declined after 1960 due to the introduction of the bacille Calmette-Guérin (BCG) vaccine, the use of effective antituberculous chemotherapy, and

improvements in public health. However, from 1984 to 1989, the risk for developing a tuberculous infection increased by 6.2% [7-9].

Diagnosing pulmonary TB in the pediatric population is challenging. The symptoms of pediatric TB infection are often non-specific or absent. Adequate specimens for diagnosis are usually difficult to obtain in children younger than 8 years due to a paucity of sputum [4,10,11]. Even in tertiary care centers, a definitive diagnosis is established in no more than 30% to 40% of patients [12,13]. For this reason, the diagnosis is usually based on a history of contact, positive tuberculin skin test (TST), and characteristic radiographic abnormalities [12,13].

This retrospective study was performed to evaluate the demographic characteristics and clinical features of pediatric TB in southern Taiwan.

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Methods

The medical charts of 103 pediatric patients younger than 15 years with a diagnosis of TB between January 1992 and May 2002 were included in the study. Ninety patients had pulmonary tuberculosis (PTB) and 13 had extrapulmonary tuberculosis (EPTB). All patients were admitted to the pediatric ward at the Kaohsiung Veterans General Hospital (KVGH), Kaohsiung, Taiwan. The following data were recorded for all patients: demographic characteristics, including age and sex; past history of BCG vaccination and contact history of active TB; clinical manifestations of cough for more than 2 weeks and fever; reported site of infection; tuberculous culture and other diagnostic findings, including acid-fast bacilli [AFB] smear, drug susceptibility, TST, and histopathologic biopsy results; and treatment regimens. Physical examination, previous TB diagnosis, household TB contact, clinical symptoms, and demographic data were analyzed. Previous BCG vaccination was confirmed by the presence of a scar on the left upper arm.

Patients with a positive TB culture from gastric aspirate or sputum, or positive AFB smear from clinical specimens were classified as having definitive TB. Patients were classified as having probable TB if they met ≥ 2 of the following criteria: positive TST (induration of ≥ 10 mm); suggestive clinical features consistent with TB; direct household contact with an individual known to have TB infection; radiographic findings (hilar lymphadenopathy, miliary shadows) compatible with TB; histological appearance of biopsy material resembling TB-affected tissue (granulomatous tubercles or caseous necrosis); or good response to ≥ 2 anti-TB drugs. Patients with previously verified TB or who were suspected to have received previous treatment were excluded.

Statistical analysis

All data were encoded and analyzed using the Statistical Package for the Social Sciences for Windows (Version 11.0; SPSS, Inc., Chicago, IL, USA).

Results

Demographic data

Between January 1992 and May 2002, a probable or confirmed diagnosis of TB was made for 103 children aged 0 to 14 years. Ninety patients (87.4%) had PTB and 13 (12.6%) had EPTB. The percentage of girls was 52.4%. The mean \pm standard deviation (SD) age of the children at diagnosis of PTB and EPTB was 6.0 ± 4.2 years and 4.5 ± 5.4 years, respectively. All patients had received BCG vaccination before the onset of symptoms, except for 1 patient who had miliary TB. The percent of patients with a household TB contact was 44.4% for patients with PTB and 7.7% for patients with EPTB (Table 1). The age at which related signs or symptoms were first noted ranged from 1 month to 14 years and 10 months (Fig. 1). TB in children aged 0 to 4 years most commonly involved the lung (53.3%) or the extrapulmonary region (69.2%) [Table 1].

Clinical presentations

The most common symptoms of PTB were cough for 2 weeks (81.1%) followed by fever (33.3%); 11.1% of children were asymptomatic (Table 2). The most frequent sites of EPTB were bone ($n = 4$) and cervical lymph nodes ($n = 4$), followed by the central nervous system (CNS; $n = 2$), miliary TB ($n = 2$), or pleura ($n = 1$). Two children with EPTB (1 in the cervical lymph nodes and the other in the CNS) had pulmonary involvement.

Table 1. Demographic characteristics and clinical features of 103 children with tuberculosis from 1992 to 2002.

Parameter	Pulmonary	Extrapulmonary	Total (n = 103)
	tuberculosis (n = 90)	tuberculosis (n = 13)	No. (%)
	No. (%)	No. (%)	
Age (years; mean \pm SD)	6.0 \pm 4.2	4.5 \pm 5.4	5.6 \pm 4.5
0-4	48 (53.3)	9 (69.2)	57 (55.3)
4-9	21 (23.3)	1 (7.7)	22 (21.3)
10-14	21 (23.3)	3 (23.1)	24 (23.3)
Female	46 (51.1)	8 (61.5)	54 (52.4)
Bacille Calmette-Guérin vaccine	90 (100)	12 (92.3)	102 (99.0)
Tuberculosis contact	40 (44.4)	1 (7.7)	41 (39.8)
Tuberculin test, induration			
<10 mm	24 (30.4)	5 (62.5)	29 (33.3)
≥ 10 mm	55 (69.6)	3 (37.5)	58 (66.7)

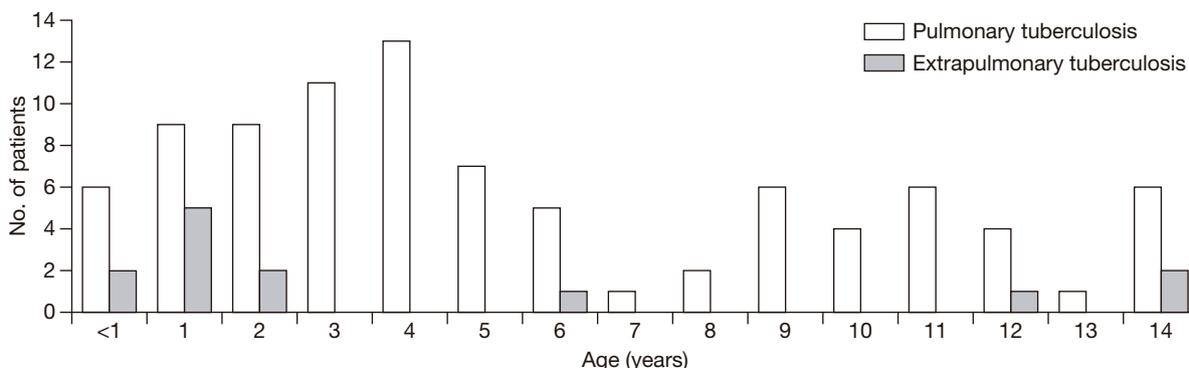


Fig. 1. Age distribution of 103 patients with tuberculosis younger than 15 years diagnosed from 1992 to 2002.

Tuberculin skin test, detection of *Mycobacterium tuberculosis*, and histopathology

The results of TST were stratified into 2 groups of induration (I) <10 mm or ≥10 mm. TST (I ≥10 mm) was positive in 69.6% (55/79) of patients with PTB, among which 63.6% (35/55) had I >15 mm. This result was reversed in patients with EPTB, with only 37.5% (3/8) of patients having I ≥10 mm (Table 1). Children with PTB had lower positive AFB rate (40.0%) and *Mycobacterium tuberculosis* (MTB) culture rate (27.8%), but more than half of the patients with EPTB had positive AFB (53.8%) and MTB culture (61.5%) [Table 3]. Eighty percent of the patients with a household TB contact had positive TST results. A similar number

of patients with positive TB culture had positive TST (52.0%) and negative TST (48.0%) results (Table 4). All patients (n = 9) who had tissue biopsy had caseous necrosis.

Treatment regimens and prognosis

All children who had PTB were treated with at least 2 anti-TB drugs for 6 to 9 months. Twenty three patients with clinically diagnosed or culture-proven PTB defaulted follow-up. One patient with PTB died despite anti-TB therapy. Two patients had infections that were resistant to anti-TB drugs (isoniazid and rifampicin, and isoniazid and streptomycin). The drug resistance rate for culture-proven PTB was 8.0% (2/25). Eleven

Table 2. Symptoms and signs of 103 patients with tuberculosis.

Symptom	Pulmonary tuberculosis (n = 90) No. (%)	Extrapulmonary tuberculosis (n = 13) No. (%)	Total (n = 103) No. (%)
Cough	73 (81.1)	4 (30.8)	77 (74.8)
Fever	30 (33.3)	5 (38.5)	35 (34.0)
Asymptomatic status	10 (11.1)	0 (0)	10 (9.7)
Chest pain/hemoptysis/dyspnea	10 (11.1)	1 (7.7)	11 (10.7)
Abdominal pain/vomiting/diarrhea	8 (8.9)	0 (0)	8 (7.8)
Runny/stuffy nose	5 (5.6)	0 (0)	5 (4.9)
Neck mass	0 (0)	4 (30.8)	4 (3.9)
Bone swelling/pain	0 (0)	3 (23.1)	3 (2.9)
Seizure	0 (0)	2 (15.4)	2 (1.9)

Table 3. Mycobacteriology of pediatric pulmonary tuberculosis and extrapulmonary tuberculosis.

Variable	Pulmonary tuberculosis (n = 90) No. (%)	Extrapulmonary tuberculosis (n = 13) No. (%)	Total (n = 103) No. (%)
Positive AFB smear and positive MTB culture	5 (5.6)	5 (38.4)	10 (9.7)
Positive AFB smear and negative MTB culture	31 (34.4)	2 (15.4)	33 (32.0)
Negative AFB smear and positive MTB culture	20 (22.2)	3 (23.1)	23 (22.3)
Negative AFB smear and negative MTB culture	34 (37.8)	3 (23.1)	37 (35.9)

Abbreviations: AFB = acid-fast bacilli; MTB = *Mycobacterium tuberculosis*.

Table 4. Percent of patients with tuberculous household contact, positive acid-fast bacilli smear and positive tuberculous culture by tuberculin skin test.

Induration	Positive tuberculous contact (n = 40) No. (%)	Positive AFB smear (n = 34) No. (%)	Positive MTB culture (n = 25) No. (%)
<10 mm	8 (20.0)	20 (58.8)	12 (48.0)
≥10 mm	32 (80.0)	14 (41.2)	13 (52.0)

Abbreviation: AFB = acid-fast bacilli; MTB = *Mycobacterium tuberculosis*.

of the 13 children with EPTB were given 2 or more anti-TB drugs for 12 to 18 months. The remaining 2 patients did not receive treatment. No drug resistance or mortality was noted among the treated EPTB patients. All patients who continued treatment in the outpatient department improved during the follow-up period.

Discussion

Despite the gradual worldwide decrease in morbidity and mortality from TB since 1960, there has been an apparent resurgence in the incidence of TB in Taiwan during the 1990s [9,14-16]. In young children in the United States, the estimated protective efficacy rates of the BCG vaccine ranges from 52% to 100% for the prevention of tuberculous meningitis and miliary TB, and from 2% to 80% for the prevention of pulmonary TB [17]. Whether the high BCG vaccination rate in Taiwan contributed to the decline in childhood TB after 1960 remains unclear due to lack of formal studies.

The most prevalent age for TB infection in this study was between 0 and 4 years. This result is comparable with previous reports [5,9,14]. Children aged between 0 and 4 years had case rates 2 to 4 times those of children aged 5 to 14 years in a previous study from the United States [5]. In this study, case rates of TB in children aged 0 to 4 years were 1.2 times higher than for those aged 5 to 14 years. The finding that 87.4% of children had pulmonary TB and 12.6% had extrapulmonary TB are similar to a previous study from the United States, which found rates of 75% and 10% for PTB and EPTB, respectively [18].

Although TST is a widely used test, it is not easy to read. A previous study found that about 20% of medical health care providers in a pediatric clinic misread a 15-mm TB skin test reaction as <10 mm [19]. Guidelines published by the American Thoracic Society stipulate that I ≥5 mm should be considered as positive only for HIV-positive patients, recent contacts of patients with TB, patients with fibrotic changes on

chest radiograph consistent with old TB, and patients who have had organ transplants and other immunosuppressed patients [20]. Using the traditional 10-mm cut-off, all vaccinated patients with a positive TST are considered to be infected. The TST remains a valuable tool for the evaluation of household contacts and suspected TB in BCG-vaccinated patients [21]. This was demonstrated by the finding in this study that 69.6% of children with PTB had I ≥10 mm. Hence, a positive TST provided an important clinical clue to identifying PTB in this study.

Children who live with adults known to have active TB are at risk for developing TB. Most contacts are immediate relatives, usually household members [22]. In this study, there was a high proportion (44.4%) of household contacts in the PTB group. It was also noted that 80% of the patients with TB with a household contact had a positive TST. Based on this finding, household contact with a person known to have TB infection appears to be an important factor for contracting PTB in southern Taiwan.

In previous studies, approximately 50% of children with active PTB were asymptomatic, especially when diagnosed early such as often occurs during a contact investigation of an infectious source [23,24]. The remaining children with PTB have non-specific symptoms and signs, including cough, fever, weight loss, vomiting, and diarrhea [18,24]. In this study, the most common manifestation of PTB was cough (81.1%), followed by fever, and other chest complaints. Guillermo et al proposed that the triad of cough lasting for more than 2 weeks, fever, and a Mantoux reaction ≥10 mm was highly predictive of culture-positive PTB among children in a low-income Peruvian population [10]. A positive TST, contact with household TB, and prolonged cough was the most common triad among the patients with PTB in this study. In a study by the Centers for Disease Control (CDC) in the USA, the leading presentations for patients with EPTB were lymphatic (16.7%), meningeal (3.3%), pleural (1.4%), miliary (1.3%), and bone/joint

(1.0%) [23]. In this series, the most frequent locations of EPTB were cervical lymph node (3.9%) and bone (3.9%). However, the size of the EPTB group ($n = 13$) was too small to expect consistency with the CDC data [23]. A previous study from northern Taiwan found a high prevalence of bone involvement in childhood TB, accounting for 56% of TB infections in children younger than 5 years [9].

In a previously reported pediatric series, 25% to 40% of specimens tested were found to be culture positive for MTB [6,12,13]. The positive culture rate of MTB in this series (32%) was within this range. Moreover, smear-positive TB infection rates were between 3% and 16% in some reports [6,23]. In this series, the recovery rate for patients with AFB-positive infection was 41.7%.

In conclusion, this study found that prolonged cough, household TB contact, and a positive TST were a triad of factors characteristic of children with PTB in southern Taiwan. Younger age was associated with higher morbidity.

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