

CHILDHOOD TUBERCULOSIS: A REPORT OF 2,205 CASES*

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SUMMARY: Göçmen A, Cengizlier R, Özçelik U, Kiper N, Şenuyar R. (Chest Diseases Unit, Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey). Childhood tuberculosis: a report of 2,205 cases. Turk J Pediatr 1997; 39: 149-158.

A total of 2,205 children with the diagnosis of tuberculosis followed at Hacettepe University İhsan Doğramacı Children's Hospital between the years 1972 and 1992 were investigated in this retrospective study. Sixty-two percent of the patients were less than six years old. There was no gender preponderance among the cases. Thirty-four percent of the patients had predisposing diseases for tuberculosis, such as malnutrition, measles and pertussis. Thirty-five percent of the patients had a history of contact with a tuberculous patient. The most common type of tuberculosis was pulmonary (39%), but extrapulmonary cases outnumbered pulmonary tuberculosis patients. Thirty-three percent of the patients had been vaccinated with BCG. The Mantoux test was found positive in 62 percent of patients. The tuberculous culture was found to be positive in the sputum of 28 percent of pulmonary tuberculosis cases. Patients were treated with daily (59%) or intermittent (41%) antituberculous therapy regimens. The response to treatment was excellent. Relapse was observed in five cases. Mortality from tuberculosis was eight percent, 23 percent of which were from tuberculous meningitis. Although there was a decrease in the number of children with tuberculosis seen at our hospital between 1972 and 1992, the prevention and control of tuberculosis are still significant health problems for our country. *Key words: tuberculosis, children.*

Because of its high morbidity and mortality rates, tuberculosis (TB) remains a major public health concern for the world. In children less than 15 years of age in developing countries, 1.3 million cases and 450,000 related deaths occur annually¹. Despite the numerous efforts to control TB in developed countries, the disease is still considered to be a major health problem-especially in urban areas².

Significant progress in the control of TB has been made in Turkey, but the disease is still one of the most significant public health problems. The aim of this study was to evaluate the clinical and laboratory features of TB in 2205 children at Hacettepe University İhsan Doğramacı Children's Hospital between the years 1972 and 1992.

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Material and Methods

The records of 2205 patients with the diagnosis of TB between 1972 and 1992 at Hacettepe University İhsan Doğramacı Children's Hospital, which is a tertiary care hospital in the capital of Turkey, were reviewed retrospectively. The diagnosis criteria for TB were: clinical and radiological evidence, a history of direct contact with an adult with TB, positive Mantoux test reaction, positive bacteriology and histopathology for tuberculosis, and characteristic findings on cerebrospinal fluid, pleural fluid and ascites fluid examination.

At this institution, 5 TU ppd solution stabilized with tween 20 was used for the Mantoux testing, and induration was measured after 48-72 hours. A Mantoux response greater than 10 mm and 15 mm were considered as positive for children without BCG and with BCG, respectively.

Radiologic examination included chest roentgenogram (postero-anterior and lateral) for all children, bone and joint roentgenogram for bone and joint tuberculosis, abdominal ultrasonography for some of the abdominal tuberculosis cases, and computed tomographic scans for some of the meningeal tuberculosis cases.

Sputum, gastric aspirate, pleural fluid, pericardial fluid, urine, cerebrospinal fluid (CSF) and biopsy specimens were inoculated in Löwenstein Jensen medium. Sputum or gastric aspirate materials were collected from 712 of the patients.

Before 1978, patients were treated with a daily antituberculous chemotherapy regimen consisting of isoniazid plus rifampin plus streptomycin daily for one month, and isoniazid plus rifampin daily for 11 months. Since 1978, uncomplicated patients have received an intermittent, antituberculous chemotherapy regimen. This regimen comprised isoniazid plus rifampin plus streptomycin daily for 15 days, then isoniazid plus rifampin twice weekly for a total of nine months until the year 1986. The regimen was then changed to isoniazid plus rifampin daily for 15 days, and then the same drugs twice weekly for a total of nine months. Patients with severe tuberculous meningitis or miliary tuberculosis received daily antituberculosis therapy for nine to 12 months, with the recent addition of pyrazinamide. Corticosteroids were used in all patients with meningitis.

Results

The number of cases per year peaked in 1977 at 168. In the following years there was a gradual decrease in cases (Fig. 1). The children's ages ranged from three months to 17 years. Sixty-two percent of the cases were less than six years of age (Table I). There was no gender preponderance among the cases.

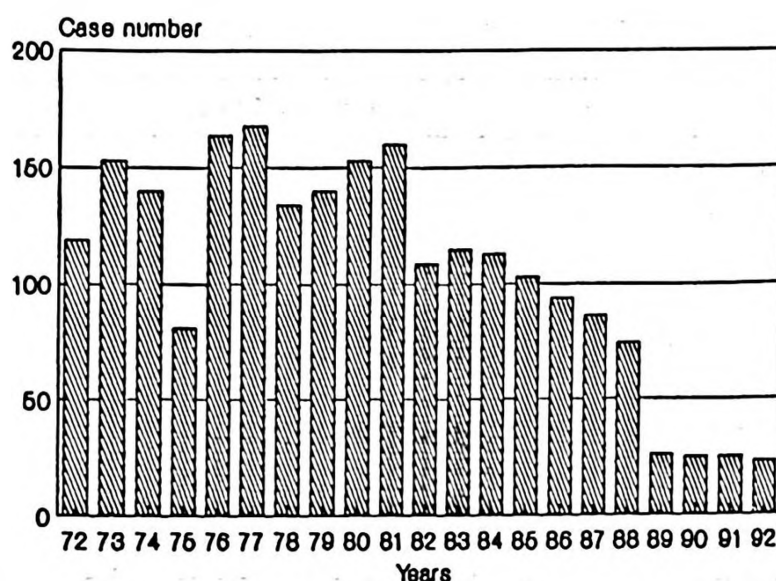


Fig. 1: Number of tuberculous cases according to year.

Table I: Distribution of Cases According to Age-groups

Age	Number of Cases	%
0-23 months	568	26
24 months-6 years	801	36
7-12 years	483	22
13 years and over	353	16
Total	2205	100

As for the predisposing diseases, 22 percent of cases had malnutrition, 11 percent had a history of measles and one percent had pertussis in the recent past.

The most common type of tuberculosis was pulmonary, followed by meningeal, miliary, pleural, lymph node, bone and joint, abdominal, pericardial, skin and genitourinary tuberculosis (Table II).

The criteria for the diagnosis of tuberculosis are listed in Table III. Thirty-five percent of the cases had a history of contact with a tuberculous patient, and 17 percent of them were living in the same household. The symptoms and physical examination findings, and the radiological findings in pulmonary TB are shown in Tables IV and V, respectively. In pulmonary TB cases, 28 percent had positive TB cultures in sputum. In extrapulmonary TB, positive cultures were obtained in 18 percent of various specimens. The Mantoux test was found to be positive in 62 percent of cases 70 percent in pulmonary and 54 percent in extrapulmonary tuberculous cases. Thirty-three percent of the patients had been vaccinated with BCG; pulmonary and extrapulmonary cases comprised 17 and 16 percent of these cases, respectively.

Table II: Sites of Tuberculosis

Site	Number of Cases	%
Pulmonary	937	39
Meningeal	537	22
Miliary	237	10
Pleurisy	186	8
Lymph node	174	7
Skeletal	173	7
Intraabdominal	93	4
Pericardial	45	2
Skin	18	1
Genito-urinary	13	0.5
Total	2413*	

* In some patients tuberculosis were detected at more than one site.

Table III: Criteria for the Diagnosis of Tuberculosis

	Pulmonary tuberculosis	Meningeal tuberculosis	Miliary tuberculosis	Pleural tuberculosis	Lymph nodes tuberculosis	Bone and joint tuberculosis	Abdominal tuberculosis	Pericardial tuberculosis	Skin tuberculosis	Genito-urinary tuberculosis
Criteria	n: 937 (%)	n: 537 (%)	n: 237 (%)	n: 186 (%)	n: 174 (%)	n: 173 (%)	n: 93 (%)	n: 45 (%)	n: 18 (%)	n: 13 (%)
Clinical	937 (100)	537 (100)	237 (100)	186 (100)	174 (100)	173 (100)	93 (100)	45 (100)	18 (100)	13 (100)
Radiologic	937 (100)	141 (26)	237 (100)	186 (100)	18 (10)	173 (100)	46 (50)	45 (100)	1 (5)	7 (53)
PPD +	656 (70)	209 (39)	19 (8)	148 (80)	131 (75)	149 (86)	76 (82)	40 (89)	12 (67)	13 (100)
Contact	347 (37)	302 (56)	116 (49)	41 (22)	9 (5)	11 (6)	3 (3)	16 (14)	2 (11)	4 (30)
Bacteriologic	262 (28)	126 (23)	42 (18)	14 (8)	9 (5)	43 (25)	12 (13)	15 (33)	2 (11)	2 (15)
Pathologic	4 (0.4)	-	2 (1)	-	60 (34)	35 (20)	8 (7)	7 (16)	2 (11)	4 (30)

Table IV: The Symptoms and Physical Examination Findings in Pulmonary Tuberculosis

Finding	Number of Cases	%
Fever	750	80
Cough	637	68
Abnormal breath sounds	440	47
Sweating	363	39
Anorexia and weight loss	365	39
Weakness	281	30
Peripheral lymphadenopathy	234	25
Normal findings	197	21
Hepatosplenomegaly	169	18
Dyspnea/respiratory distress	112	12
Erythema nodosum	19	2

Total number: 937

Table V: Radiological Findings of Pulmonary Tuberculous Patients

Finding	Number of Cases	%
Hilar lymphadenopathy	402	43
Infiltration	356	38
Pleural effusion	122	13
Miliary spread	84	9
Atelectasis	28	3
Calcification	28	3
Cavern	19	2

Total number: 937

The cases were treated with daily or intermittent antituberculous therapy regimens (Table VI). Patients who completed the therapy numbered 1,742 (79%), and the clinicoradiologic response to treatment was observed to be excellent. Relapse was noted in five patients: one with pulmonary tuberculosis and Hodgkin's disease, one with pulmonary tuberculosis and cyclic neutropenia, one pulmonary tuberculosis case, and two lymph-node tuberculosis patients. Two cases of relapse were in the intermittent therapy group. These patients were successfully retreated with intermittent anti-tuberculous chemotherapy. Serious side effects of the drugs were not observed in any patient. A transient increase in liver enzymes was observed in 67 patients, 12 of them in the intermittent therapy group. These high levels returned to normal with the cessation of therapy or by decreasing the drug levels for a while. Changing the drug regimen or stopping the antituberculous therapy for a long time was not necessary in any case.

Table VI: Treatment of Patients

Treatment	Site of Tuberculosis	
	Pulmonary (%)	Extrapulmonary (%)
Daily*	254 (27)	1166 (79)
Intermittent a**	646 (69)	280 (19)
b***	37 (4)	30 (2)
Total	937 (100)	1476 (100)

*: Isoniazid plus rifampin plus streptomycin or pyrazinamide daily for one month, and isoniazid plus rifampin daily for 8 to 11 months.

** : Isoniazid plus rifampin plus streptomycin daily for 15 days, then isoniazid plus rifampin twice weekly for a total of 9 months.

*** : Isoniazid plus rifampin daily for 15 days, then the same drugs twice weekly for a total of 9 months.

According to the obtainable data from the patients who were followed up, the mean mortality rate was eight percent for all tuberculosis patients, the highest found in tuberculous meningitis (23%) (Table VII). Of the patients who died, two pulmonary tuberculosis patients had congenital heart disease and malnutrition, one pulmonary tuberculosis patient had chronic renal failure, one bone and joint tuberculosis patient had chronic renal failure, and two bone and joint tuberculosis patients had malnutrition.

Table VII: Distribution and Ratio of Tuberculosis Mortality

Site of Tuberculosis	Number of Patients	Number of Deaths	% of Deaths
Meningeal	537	124	23
Miliary	237	25	11
Abdominal	93	7	8
Skeletal	173	7	4
Pericardial	45	6	13
Pulmonary	937	5	0.5
Pleural	186	—	—
Lymph node	174	—	—
Skin	18	—	—
Genito-urinary	13	—	—
Total	2413	174	8

Discussion

The number of TB cases that were admitted to our hospital was 119 in 1972. This number increased to 168 in 1977 and decreased to 23 in 1992. During this period the total number of patients admitted to our hospital each year did not vary significantly, the mean being 135,000 patients. This decrease in TB cases over the years may be due to the diagnosis and treatment of the disease by peripheral health units. The overall incidence of TB in Turkey has also decreased in recent years. According to data from the Turkish Ministry of Health, the number dropped to 51/100,000 in 1988 from 108 in 1971³⁻⁵. The other change was in the pulmonary-extrapulmonary TB distribution. Between the years 1972 and 1981, the prevalences of pulmonary and extrapulmonary TB were 54 and 46 percent, respectively. Since 1982, there has been a decrease in pulmonary TB cases from 54 to 38 percent, while there has been an increase in extrapulmonary TB cases from 46 to 62 percent. Similar changes have been reported from other countries: while there is an increase in extrapulmonary TB, the incidence of pulmonary TB is decreasing⁶⁻⁸.

Tuberculosis is seen relatively more frequently in early childhood and the elderly⁸⁻¹⁰. Sixty-two percent of our patients were less than six years of age. This number was also compatible with that observed in other countries¹¹⁻¹⁴.

Resistance to tuberculosis may be lowered by several factors, such as malnutrition, certain infections (measles, varicella, pertussis, HIV and certain other viral illnesses), corticosteroids and other immunosuppressive therapy, stress and hormonal changes. Twenty-two of our patients had malnutrition, 11 percent had a history of measles, and one percent had pertussis in the recent past. Bhakoo and colleagues¹¹ described a 22 percent incidence of measles, 18 percent pertussis and five percent incidence of varicella in 149 tuberculosis patients. In Hernandez and colleagues' study¹⁵, the incidence of malnutrition was 82 percent in 277 meningeal tuberculous patients.

An important factor in the spread of the disease is the presence of undiagnosed cases. A history of contact with some one with TB was present in 35 percent of cases. In a previous study done in Turkey, a history of contact was found in 42 percent of patients¹⁶. Reports from other countries reported this figure at 80 percent¹², 60 percent¹⁷ and 44 percent¹⁸, and contact with TB has been stressed as an important factor in the spread of the disease. In India, where the incidence of tuberculosis is high, a history of contact was found to be 10-15 percent¹¹ and 30 percent¹⁹. The reason for this low rate of contact was thought to be due to concealment of the history of contact because of feelings of guilt expressed at the occurrence of disease in the family or because the presence of the disease was unknown¹¹. It is important, therefore, that patients be persistently questioned about TB contact and that family members be examined for TB.

Tuberculosis may present with a variety of symptoms and physical examination findings. Symptoms and physical findings seen among our pulmonary tuberculous patients were similar to those of other reports²⁰⁻²³. Infants and young children with pulmonary tuberculosis were more likely to have symptoms such as cough, fever, weight loss, and wheezing or decreased breath sounds¹⁴. In our study, clinical findings, including signs and symptoms, played an important role in the diagnosis of tuberculosis.

The predominant radiological findings in pulmonary tuberculosis patients were lymphadenopathy (43%) and parenchymal infiltration (38%). In different studies, lymphadenopathy was by far the most common abnormality in pulmonary tuberculosis patients' x-ray findings (100% in the study by Abernathy and colleagues²³ and 93.5% in Pineda and colleagues²⁴ study). In the study of Biddulph and colleagues²⁶ this finding was similar to that in our study at 53 percent of patients.

A positive culture was detected in 28 percent of pulmonary tuberculosis cases.

A positive culture, generally associated with low ratios in childhood tuberculosis, was reportedly detected in seven to 35 percent cases in previous studies^{13, 26}. The positive culture rate was very low in extrapulmonary tuberculosis because of difficulties in obtaining samples.

The Mantoux test was positive in 62 percent of cases. In tuberculous meningitis 39 percent and in miliary TB only eight percent had positive Mantoux test reactions. Similar results have been reported in the medical literature: ppd was found positive in only 16 percent of patients with TB meningitis⁹, and 41 percent in miliary TB⁸.

Thirty-three percent of our patients had been vaccinated with BCG. In the literature, the protective efficacy of BCG vaccination is controversial and ranges from zero to 80 percent²⁷. However, it has been stressed that in childhood the vaccination protects against serious complications tuberculous meningitis^{3, 18, 27, 28}.

We used intermittent antituberculous chemotherapy for a large patient group and found it to be as effective as daily treatment. The results of intermittent antituberculous chemotherapy in children have been reported as successful in a number of studies^{23, 25, 29}. Relapse was observed in five patients in the late period, and two of them were immunocompromised. It is well known that poor compliance with therapy and immunosuppression play important roles in the response to antituberculous therapy and relapse. Serious side effects were not observed in any patient. The explanation for the rarity of side effects could be the use of drugs at low dosages and young age-groups.

The most serious complication that led to a fatal outcome was TB meningitis, with an incidence of 23 percent. The mortality associated with TB meningitis has been reported to be 12 to 72 percent^{6, 23, 30}. The overall mortality rate in our series was eight percent. According to data released by the Turkish Ministry of Health, mortality due to TB is 3.68 per 100,000. While in the 1950s TB was the leading cause of death in Turkey, in 1987 it had dropped to 18th place^{3, 28}. The reason for our high mortality rate may be the fact that complicated cases are referred to our hospital. Consequently, complications such as TB meningitis, are seen more frequently.

There has been a decrease in TB cases in our hospital over the last 21 years. The ratio between pulmonary and extrapulmonary involvement has shifted slightly towards extrapulmonary disease. Predisposing factors such as infectious diseases, malnutrition and contact with another person with TB play important roles in the occurrence and spread of the disease. With a mortality rate of eight percent, the prevention and control of TB are still important health concerns.

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