

Original Article

Evaluation of diagnostic components and management of childhood pulmonary tuberculosis: a prospective study from Istanbul, Turkey

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Abstract

Introduction: The diagnosis of childhood tuberculosis is difficult and most of the patients are diagnosed clinically. The objective of this study is to reveal the diagnostic and therapeutic components of childhood pulmonary tuberculosis and to analyze the changes that occurred in our country over the years.

Methodology: All patients diagnosed with tuberculosis between 2006 and 2016 were included. Demographic characteristics, diagnostic and treatment outcomes were recorded and patients were followed up prospectively.

Results: A total of 492 patients were included in the study. 97% had Bacillus Calmette-Guerin vaccine, 36% were diagnosed with microbiologically-confirmed tuberculosis and 64% were diagnosed with clinically-proven tuberculosis. 94% of the patients had symptoms consistent with tuberculosis, all patients had radiologic findings, 74% had a history of tuberculosis contact and 63% had tuberculin skin test positivity. The diagnoses included primary tuberculosis in 62%, secondary tuberculosis in 21%, progressive primary tuberculosis in 13% and miliary tuberculosis in 4%. 48% of the patients received a treatment regimen containing three drugs as the initial treatment, and drug-related side effects developed in 12%. Isoniazid resistance was detected in 13% of the patients and rifampicin resistance was detected in 8%. None of the patients died due to tuberculosis. In the last 50 years in Turkey, the rates of *Bacillus Calmette-Guerin* vaccination and diagnosis of tuberculosis cases have increased and the mortality rates have decreased over the years.

Conclusions: Our study is one of the few prospective studies and revealed the differences between the recent data and the past 50 years in childhood tuberculosis in Turkey.

Key words: Tuberculosis; child; drug resistance.

J Infect Dev Ctries 2022; 16(1):112-119. doi:10.3855/jidc.14505

(Received 14 December 2020 – Accepted 25 March 2021)

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Introduction

Tuberculosis (TB) is still an important public health problem in Turkey and on a global scale. According to the 2019 data of the World Health Organization (WHO), there are a total of 1,000,000 pediatric TB cases worldwide [1]. Since the bacteria that cause TB are usually transmitted from adults to children, a decrease in childhood tuberculosis indicates the effectiveness of adult tuberculosis control programs [2,3]. Childhood tuberculosis is often treatable if it is diagnosed promptly. Although children are considered a sensitive and priority group in the global community regarding to the diagnosis and treatment of tuberculosis, pediatric cases may be undiagnosed since public health approaches are generally based on sputum positivity [4].

WHO recommends conducting studies including documentation of the methods for diagnosing childhood tuberculosis in different social and epidemiological conditions [5]. It seems unlikely that WHO's EndTB goal will be achieved if the challenges of diagnosis, treatment and prevention in childhood tuberculosis are not resolved. Therefore, there is a need for studies that evaluate age-compatible clinical diagnostic methods, pediatric prevalence surveys, and drug regimens in different settings. Researches and investments regarding to pediatric tuberculosis and access to treatment must be a global priority [4-6].

The diagnosis of TB differs in children compared to adults in many regards. While the diagnosis of TB is based mainly on microbiology in adults, it is usually made with clinical findings in children as bacilli counts

are lower. Radiological findings, history of TB contact, tuberculin skin test (TST) positivity and response to therapy play a role besides clinical findings [3,7].

According to the “Fighting with Tuberculosis in Turkey 2018” report, the diagnosis and treatment are still challenging, though the number of new cases decreased in children as well as in adults [2].

Since the studies on childhood pulmonary TB (PTB) in our country are mostly retrospective, some data about diagnosis, treatment, drug side effects and sequelae are missing. Most of the studies include both cases of PTB and extra-pulmonary TB (EPTB) [8-15]. We analyzed childhood PTB cases prospectively in terms of diagnostic components, treatment details and outcomes, recurrence status, drug side effects and sequelae. The results were also compared with the results obtained within the last 50 years. Our study is one of the few prospective studies on this issue and revealed the differences between the recent data and the past 50 years in childhood TB in Turkey.

Methodology

Patient selection

All children diagnosed with PTB at Bezmialem Vakif University, Sureyyapaşa Research and Training Hospital and Maltepe University between September 2006 and April 2016 were included in the study. The demographic, radiological, microbiological and treatment data of the patients were recorded.

A brief history of symptoms and TB contact was obtained, and detailed physical examination was performed.

Radiology

An antero-posterior chest radiograph was obtained in all patients. Computed tomography (CT) of the thorax was obtained only in the presence of suspicious findings on chest X-ray and when chest radiograph was inconsistent for differential diagnosis. Patients were

divided into primary, progressive primary, secondary and miliary groups according to their radiological appearances [3,7].

TST positivity and immunological tests for TB

TST was performed in all patients and induration was considered positive if it was ≥ 15 mm in patients who had BCG vaccination, ≥ 10 m in unvaccinated subjects and ≥ 5 mm in immunosuppressed subjects. Interferon gamma release assay (IGRA) was performed in patients with positive clinical and radiological findings who were clinically suspected of having PTB, but who did not have a history of TB contact and TST positivity.

Microbiological examination

At least one microbiological sample was obtained from each patient. For microbiological examination, sputum sample was obtained if the child could expectorate or gastric aspirates were obtained on 3 consecutive days in children who could not produce sputum [3,7,16,17].

Bronchoscopy

Bronchoscopy was performed in patients who had airway involvement at initial diagnosis or clinical and radiological findings resistant to therapy, and bronchoalveolar lavage (BAL) fluid was obtained [3,7,18,19].

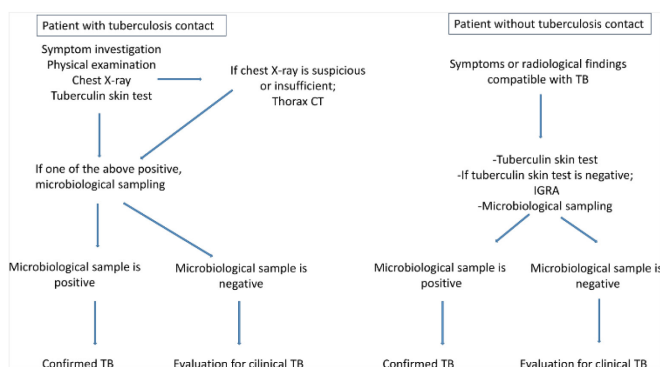
Patient definition

Patients, whose TB diagnosis was confirmed microbiologically, were defined as “confirmed TB”. The remaining patients were defined as “clinically-proven TB” based on radiologic findings consistent with TB, history of TB contact, TST positivity and response to TB treatment [3,7,16] (Figure 1).

Treatment and follow-up

The patients with mild PTB were given triple treatment composed of isoniazid, rifampicin and pyrazinamide in accordance with the diagnosis and treatment guidelines [3,7]. Four-drug therapy was initiated, including ethambutol, in patients who had severe PTB or who were bacillus-positive. No patient received streptomycin treatment. Ophthalmic examinations were performed before and after ethambutol treatment. Treatment was switched to dual therapy at the end of the second month if clinical and radiological improvement could be achieved and terminated at the end of the sixth month. Initial treatment was extended to three months for the patients who were still bacillus-positive at the second month of

Figure 1. Diagnosis flow chart for our patients.



treatment. Treatment of some patients, who had severe clinical and radiological findings, was extended to 9 months in accordance with the guidelines [3,7,20,21]. Drug susceptibility testing could not be performed for all positive cultures due to technical and laboratory insufficiency during the initial years, but it was performed for all patients thereafter. Results of drug susceptibility tests, treatment outcomes and recurrence states were recorded for all patients. The patients were followed up for drug side effects. All medications were interrupted when hepatotoxicity developed and continued after liver function tests became normal. The medications were administered after re-sensitization if hepatotoxicity developed again.

Table 1. Clinical, radiological and diagnostic characteristics of the patients.

Age (Median)	130 months
Minimum	4 months
Maximum	16 years
Age distribution	
0-1 year [n (%)]	30 (6)
1-4 years [n (%)]	69 (14)
5-10 years [n (%)]	152 (31)
>10 years [n (%)]	241 (49)
Gender	
Female [n (%)]	265 (54)
Male [n (%)]	227 (46)
Symptoms	
Cough [n (%)]	398 (81)
Fever [n (%)]	162 (33)
Weight loss and fatigue [n (%)]	123 (25)
Hemoptysis [n (%)]	44 (9)
Sweating [n (%)]	29 (6)
Wheezing [n (%)]	10 (2)
Erythema nodosum [n (%)]	10 (2)
Duration of symptoms (mean±standart deviation)	2 ± 2.3 months
Physical examination	
Normal	167 (34)
Fine or rough crepitating rales	266 (54)
Reduced respiratory sounds	59 (12)
BCG vaccination [n (%)]	479 (97)
Chest radiology	
Lobar infiltration[n (%)]	236 (48)
Cavitation [n (%)]	89 (19)
Lymph-adenopathy [n (%)]	72 (15)
Broncho-pneumonia [n (%)]	54 (11)
Pleury [n (%)]	49 (10)
Miliary appearance [n (%)]	20 (4)
Radiological diagnosis of TB cases	
Primary TB [n (%)]	304 (62)
Secondary TB [n (%)]	105 (21)
Progressive primary TB [n (%)]	63 (13)
Miliary TB [n (%)]	20 (4)
Case definition	
Microbiological confirmed TB	176 (36)
Clinical TB	316 (64)

Table 2. Positivity rate of the diagnostic components.

	n (%)
Radiology	492 (100)
Clinic	462 (94)
Contact	364 (74)
TST positivity	305 (62)
Microbiology	176 (36)

The patients were evaluated at the time of diagnosis and at the 1st, 2nd, 3rd, 6th, 9th, 12th, 18th and 24th months after that. They were followed up in terms of sequela lesions. Follow-up was discontinued if the patient did not have any problem after 24 months.

Statistical analysis and ethical considerations

Statistical analyses were done using SPSS 21 program. Local ethics committee approval (18.08.2011, decision number: 11/9) was obtained from Bezmialem Vakif University and informed consent was obtained from the parents of the patients before study entry.

Results

Demographic characteristics and symptoms

Demographic characteristics of the patients are presented in Table 1. Among patients, 54% were female and the median age was 130 months (25-75 percentile: 78-156 months). One or more symptoms were detected in 94% of the patients. Cough, fever and weight loss were the most common symptoms (Table 1). All patients, who did not have any complaints, were found to have a history of TB contact and were diagnosed with radiological and/or microbiological findings consistent with TB. Physical examination was normal in 34% of the patients, 54% had fine and rough crackles, and respiratory sounds were decreased in 12% (Table1).

TB contact and TST positivity

History of TB contact was obtained in 74% of the patients; 74% had household contact and 25% had contact with close relatives. TST positivity was detected in 62% of the patients (Table 2). IGRA was performed in 48 of 128 patients without TB contact and TST was negative. IGRA positivity was determined in only 9 of 48 patients ($p > 0.05$).

Radiology

Radiological findings of the patients are presented in Table 1. Of the patients, 62% had primary TB, 21% had secondary TB, 13% had progressive primary TB and 4% had miliary TB. Pleural involvement accompanied in 10% (n = 49) of the patients. The median age of the patients with secondary TB was 13 years (25-75, IQR = 11-14 years) and 73% of the

patients were female. The youngest patient with secondary TB was 7 years old.

A diagnosis of PTB was consistent with symptoms and radiological findings in 20 patients who did not have a history of TB contact, TST positivity or culture positivity. The diagnosis was confirmed after full recovery of the patients with TB treatment (Table 2).

Bronchoscopy

Flexible bronchoscopy was performed in 134 patients (27%). Bronchoscopy was performed because of persisting clinical and radiological findings despite TB treatment in 15% of the patients and because of suspected airway involvement in the remaining 12%. Endobronchial lesions and lymphadenopathy (LAP) causing lumen obstruction were detected in 48% of the patients (n = 64). Systemic steroid treatment was given in 42 (8%) patients who had obstructive intraluminal lesions and LAP compression narrowing the lumen by more than 2/3.

Microbiology and case definition

ARB was positive in 29% of the patients (n:145), 36% had culture positivity and these patients were identified as microbiologically confirmed TB. The remaining 64% (n = 316) were diagnosed as clinically proven TB (Table 3). One hundred and twenty patients could give sputum sample and culture positivity was found with a rate of 46% (n = 55). Gastric aspirate samples were obtained from 372 patients who could not give sputum, and culture positivity was detected in 26% (n = 97). Culture positivity was found with a rate of 28% (n = 37) in BAL samples in 134 patients who underwent bronchoscopy. The combination of gastric aspirate and BAL fluid cultures revealed 13 more patients with culture positivity. With this combination,

the rate of culture positivity was found to be significantly increased compared to gastric aspirate culture or BAL fluid culture alone ($p = 0.02$).

Contribution of diagnostic components to the diagnosis of TB

In our study, the contributions of diagnostic components of TB and their combinations were analyzed (Table 3). Thirty six percent (36%) of the cases were microbiologically confirmed. When the patients with clinically-proven diagnosis were evaluated, radiological findings, a history of TB contact or immunological findings were found to be present in association besides TB-related complaints (Table 3). Another essential diagnostic component, response to therapy, was observed in all patients.

Treatment, drug side effects and drug resistance

Triple therapy regimen was initiated in the patients who had mild PTB (n = 238, 48%) and four-drug therapy was initiated in the patients who had severe TB, cavitory lesion and ARB positivity (n = 254, 52%). Ethambutol was initiated as the fourth drug in all patients. Initial treatment was extended to 3 months in 54 patients (11%) due to the absence of full clinical, radiological and microbiological recovery. Treatment was extended to 9 months in 43 patients (9%) (Table 4).

Table 3. Combinations of diagnostic components.

	n (%)
Microbiologically-confirmed cases	176 (36)
Radiology + TB Contact+ TST positivity +Microbiology	64 (13)
Radiology +TB Contact+Microbiology	54 (11)
Radiology +TST positivity+ Microbiology	34 (7)
Radiology + Microbiology	26 (5)
Clinically-proven cases	316 (64)
Radiology +TB Contact+ TST positivity	157 (32)
Radiology +TB Contact	88 (18)
Radiology +TST positivity	49 (10)
Radiology *	20 (4)
Total	492 (100)

* 14 patients had cavitory lesions and were diagnosed with full recovery with treatment. 6 patients were diagnosed based on pleural fluid findings (color, biochemical properties, elevated ADA level) and full recovery with treatment.

Table 4. Treatment, drug resistance and drug side effects of the patients.

	n (%)
Triple treatment as initial treatment *	238 (48)
Quadruple treatment as initial treatment**	254 (52)
Initial treatment prolonged to 3 months	54 (11)
Total treatment prolonged to 9 months	43 (9)
Total number of the patients who developed drug side effects	60 (12)
Elevated liver enzymes	34 (7)
Vomiting	26 (5)
Abdominal pain	22 (4)
Allergic reactions	10 (2)
Hemorrhagic diathesis	10 (2)
Convulsion	4 (1)
Number of patients who were examined for drug resistance	76 (15)
Single drug resistance	12 (16)
H resistance	10 (13)
S resistance	8 (10)
R resistance	6 (8)
E resistance	6 (8)
MDR	4 (5)
Treatment success	492 (100)
Recurrence	10 (2)
Number of patients who underwent lobectomy due to sequel	8 (2)

* isoniazid, rifampicin, pyrazinamide; ** isoniazid, rifampicin, pyrazinamide, ethambutol.

Drug resistance was observed in 60 patients (12%). Elevated liver enzymes, vomiting and abdominal pain were the most common drug side effects (Table 4). The drugs were completely interrupted in 40 patients (8%) due to side effects of the drugs and restarted when the findings returned to normal. However, the treatment could be restarted with resensitization as the side effects repeated in 14 patients. Treatment could be completed in all patients.

At least one drug resistance was detected in 12 of 76 patients (16%) in whom drug-resistance testing could be performed. While all patients recovered with treatment, recurrence developed in 10 patients. In the long-term follow-up, 8 patients underwent lobectomy due to sequela atelectasis, bronchiectasis and damaged lungs (Table 4). None of the patients died due to TB.

Our study results were compared with childhood TB studies conducted in our country in the last 50 years, and are presented chronologically in Table 5.

Discussion

In the current study, pediatric patients with PTB were analyzed prospectively, and demographic characteristics, diagnostic components, treatment and follow-up findings were presented comprehensively. Our study was conducted in a wide group of patients who were diagnosed with pulmonary tuberculosis. Since it was a prospective study, missing data were extremely scarce.

The results obtained from this study were compared with those of the other studies investigating childhood TB in our country, and the changes observed over the years were analyzed in Table 5.

Childhood PTB can affect all age groups. In our study, the median age was found to be 130 months, while the mean age was found to be about 8 years in other studies from Turkey. As in many studies, gender rates were found to be similar [9-11,14,15].

BCG vaccination rates have been observed to be increased over the years in Turkey. While the BCG vaccination rate was found to be 33% in the study conducted by Gocmen *et al.* [8], this rate was found to be above 90% in recent studies and in our study [14,15]. The coverage of the national vaccination program has been steadily increasing over the years. In the final national guideline, it was decided to continue BCG vaccination in our country [3].

The diagnosis of TB is divided into two categories as “confirmed TB” and “clinically-proven TB” in children. The rate of microbiologically-confirmed cases is low in childhood TB as bacilli counts and sputum yield are low [3,16]. Therefore, studies report limited microbiological results [8-11]. In three studies conducted in our country, microbiological examination was observed to be performed in all patients, and the rate of confirmed TB cases was shown to vary between 20% and 37% [12,14,15]. In our study, microbiological examinations were also performed in all patients, and the rate of confirmed TB was found to be 36%.

The diagnosis of clinically-proven TB can be made based on TB-related symptoms, radiological findings, history of TB contact, TST or IGRA positivity and response to therapy. The main TB-related symptoms include cough lasting longer than 2 weeks and fever of unknown origin lasting longer than one week. Fatigue, weight loss, night sweats are the other findings. In the literature, cough has been reported with a rate of 49-

Table 5. Childhood tuberculosis studies from Turkey.

Study	Year	Total number	Pulmonary TB number	Mean age	BCG vaccination (%)	TB contact (%)	TST positivity (%)	Microbiological positivity (%)	Drug side effect (%)	H drug resistance (%)	R drug resistance (%)	Relapse (%)	Sequel (%)	Mortality (%)
Goçmen <i>et al.</i> [8]	1972-1992*	2205	860	%62<72 months	33	31	62	28				5 patients		8
Pekcan <i>et al.</i> [10]	1994-2005*	539	285	7 years (mean)		40	55	23				%3		1.5
Güleç <i>et al.</i> [12]	2007-2008*	51	36	8 years (mean)	55	53	45	37	2	7.8				4
Turel <i>et al.</i> [11]	2004-2010*	250	162	7.8 years (mean)	70	63	53	19						
Cakir <i>et al.</i> [9]	2006-2010*	1541	847	8.8 years (mean)				35		15	9	%1		
Yesil <i>et al.</i> [15]	2005-2015*	93	48	93 months (median)	92	29	72	20	15	21	8			1
Aygün <i>et al.</i> [14]	2007-2017*	163	73	9.8 years (mean)	97	46	59	20	18				1	-
Current study	2006-2016**	492	492	130 months (median)	97	74	62	36	12	13	8	%0.2	2	-

* Pulmonary and extrapulmonary cases; ** Pulmonary TB cases.

70% [10,14] and fever has been reported with a rate of 43-53% [11,14]. In our study, cough was found with a rate of 81% and fever was found with a rate of 33%. The rate of cough was considered to be higher in our study compared to the other studies, because we addressed only PTB.

Radiological findings constitute another important component for the diagnosis of TB in children [3,16]. Radiological findings irrespective to nonspecific treatment require assessment in terms of TB. The most common radiological findings include infiltration, consolidation, lymphadenopathy and lung cavity [7,11,15]. In our study, all cases were confirmed radiologically, similar to the study conducted by Aygun *et al.* who reported radiological findings consistent with TB in all patients. Primary TB was detected to be the most common radiological diagnosis followed by adult type secondary TB accompanied by lung cavity image in our study. The youngest patient, who experienced secondary TB, was 7 years old in our study. Pleural TB was detected in 20 patients who had PTB. This study is one of the rare studies that classify PTB as primary, progressive primary and secondary TB.

As microbiological diagnosis of pediatric tuberculosis is difficult and there are many asymptomatic cases, we need some diagnostic tools. History of TB contact is one of the important diagnostic components. If there is an infection after contact with tuberculosis in the first 5 years of life, the risk of getting sick is high. In some regions of the United States, more than 50 % of the cases of pediatric tuberculosis were diagnosed during contact investigations performed for adults with infectious tuberculosis [7,11,15].

TB contact in childhood tuberculosis was detected with a rate of 29-63% in our country [11,15]. In a recent study, this rate was found to be 74% which was higher compared to the literature. The number of the patients who were detected to have TB by contact screening was shown to be increased compared to other studies [8-12,14,15]. High contact rates in our study group might be due to the prospective nature of the study. Pekcan *et al.* reported that the most common source of TB contact was first and second degree relatives, similar to Aygun *et al.* who reported household contact to be the most important source [10,14]. In our study, household contact was found with a rate of 74% and contact with relatives was found with a rate of 24%. It is concluded that, screening for TB contact is essential in the diagnosis of TB, and detailed history should be taken to prevent recall bias.

TST and IGRA positivity are other diagnostic factors. IGRA is known not to be superior to TST for

detecting latent TB [3,17]. In our national TB diagnosis and treatment guidelines, TST is primarily recommended for the diagnosis of TB. IGRA is recommended for supporting the diagnosis if TST yields negative results in patients who have suspected clinical and radiologic findings but do not have a history of TB contact [3,7]. In the literature, TST positivity is reported to vary between 45% and 72% in children diagnosed with TB [12-15]. In our study, TST positivity was found with a rate of 62%, consistent with the literature. IGRA positivity was detected in 9 of 48 patients, who did not have a history of TB contact and whose TST results were negative, and the difference was not statistically significant.

Our study is the first study that demonstrates the contribution of diagnostic components and their combinations to the diagnosis of TB. When the patients with clinically-proven TB were evaluated, it was found that radiological findings, contact history or immunological findings were found to accompany TB-related complaints in all patients except 20 cases (Table 3). Response to TB treatment is another clinical criterion for the diagnosis [16]. The diagnosis was confirmed in all of these 20 patients who responded to TB treatment.

Bronchoscopy is not routinely recommended in childhood TB. Indications for bronchoscopy include clinical and radiological findings irrespective to therapy, suspected airway involvement and not being able to make a differential diagnosis. Airway involvement is found in 41%-63% of the cases of pediatric pulmonary tuberculosis. Bronchoscopy can be useful for the diagnosis of endo-bronchial TB and airway obstruction, and BAL fluid enables microbiological examinations [3,18,23,24]. Diagnostic accuracy of the results from bronchoscopy and HRCT were evaluated in smear negative patients who were suspected of having active pulmonary tuberculosis, and the sensitivity, specificity, positive predictive value and negative predictive value of bronchoscopy alone for the diagnosis of active pulmonary tuberculosis were found to be 75.9%, 97.2%, 95.3%, and 84.3%, respectively. The combination of these diagnostic tools improved the sensitivity to 96.3% and the negative productive value to 96.2% [25]. The rates of microbiological positivity of BAL fluid was found to be equal to the rates found for gastric aspirates in some studies similar to our previous study, while they were found to be lower or higher in other studies. Combined use of BAL fluid and gastric aspirates was shown to significantly increase microbiological positivity [18,19,21,23-29].

In a recent study, disorders that narrow the airways were detected in about half of the bronchoscopies performed in accordance with the above-mentioned criteria and steroid was added to treatment. Besides, positive BAL culture was found to be a significant contributing factor in terms of diagnosis. It was concluded that bronchoscopy could be performed to support the diagnosis as shown in the literature [3,18,23,24].

In childhood TB, initial treatment should be performed using 3 or 4 drugs in accordance with the guidelines. Streptomycin is no longer a first-line drug and ethambutol is used as the 4th drug in all patients beginning from infancy [3,7,20,21]. There are few studies on treatment characteristics and follow-up in the literature. The rate of four-drug treatment varies between 37% and 68% [12,14,15]. This rate was found to be 52% in our study, consistent with other studies conducted in our country.

Children tolerate anti-tuberculosis drugs better. Side effects are observed with a rate of approximately 15%. The most common side effects include hepatotoxicity, vomiting, abdominal pain and elevated uric acid levels [14,15,30]. In our study, the rates of side effects were found to be similar to other studies, and the most common side effect was hepatotoxicity. The drugs were completely interrupted due to side effects in 40 patients and restarted when the findings returned to normal. In 14 patients, the drugs could be restarted with re-sensitization as side effects repeated. This study is one of the rare studies that provide information about drug side effects.

Drug resistance continues to be a problem in our country as well as on a global scale [31]. Isoniazid resistance was found to be 7.8% in the first study on drug resistance in our country (32). In the literature, this rate was shown to be increased in Turkey [9,5] and was found to be 13% in our study. Rifampicin resistance has not changed significantly in time and stayed around 8% [9,15,23].

TB-related mortality has not occurred recently in Turkey. While the mortality rate was found to be 8% in the study conducted by Gocmen *et al.*, it has decreased gradually in current reports [8,14,15] (Table 5). None of the patients died due to TB in our study group.

Recurrence rates are low in childhood TB [12-14], and the recurrence rate in our study was found to be 0.2%.

Childhood TB can rarely lead to sequela. Aygun *et al.* reported 2 cases of EPTB that resulted in sequela. In our study, 8 patients underwent lobectomy due to sequela. Although the rates of pleurisy were similar, the

cavity rate was 8 times higher in our series [14]. This finding might have arisen from the difference between two groups.

Conclusions

Prospective studies are important for revealing all components of diagnosis and treatment. It is established that rates of BCG vaccination and diagnosis of tuberculosis cases by way of TB screening have increased and TB mortality rates have decreased over the years compared to the last 50 years of Turkey. While isoniazid resistance increases, rifampicin resistance has stayed at the same level in our country. Regular file records would be useful for clinicians to follow up patients and course of the disease.

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Conflict of interests: No conflict of interests is declared.