



Evaluation of clinical and laboratory characteristics of childhood tuberculosis

Çocukluk çağı tüberküloz olgularında klinik ve laboratuvar bulgularının değerlendirilmesi

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The known about this topic

Tuberculosis ranks first among infectious diseases that lead to death caused by a single contagious agent worldwide. Epidemiologic data are limited in children because of difficulties in the diagnosis of tuberculosis. Extrapulmonary tuberculosis is observed more commonly in children compared with adults because of the higher risk of lymphohematogenous spread.

Contribution of the study

The association of pulmonary tuberculosis and extrapulmonary tuberculosis was found with a higher rate in the subjects whose families lived on minimum wage and in patients with growth and developmental delay. Hospitalization duration was longer in the patients who had an association of pulmonary tuberculosis and extrapulmonary tuberculosis. Hemoglobin and sodium levels were found to be significantly lower in the patients who had extrapulmonary tuberculosis.

Abstract

Aim: Tuberculosis is one of the oldest and most contagious diseases of human history. One-quarter of the world's population is infected with the tuberculosis bacillus. Childhood tuberculosis does not have a standard clinical and radiologic description. Herein, we aimed to evaluate the clinical, laboratory, and radiologic findings of childhood tuberculosis.

Material and Methods: The medical records of 216 patients hospitalized and treated with a diagnosis of TB between January 2015 and July 2019 in the Division of Pediatric Infectious Diseases in our hospital, were examined retrospectively.

Results: One hundred twenty-nine (59.7%) of 216 patients who were diagnosed as having TB were female and 87 (40.3%) were male. The age distribution of the patients was 12.3 (range, 0.33–18) years. One hundred sixty-nine patients (78.2%) had pulmonary, 34 (15.7%) had extrapulmonary, 13 had (6%) both pulmonary and extrapulmonary. One hundred forty-three (66.2%) patients had tuberculin skin test positivity. Acid-resistant bacteria were observed in 46 (21.3%) body fluid samples, and culture positivity was observed in 42 (19.4%) samples. The association of pulmonary tuberculosis and extrapulmonary tuberculosis was found with a higher rate in individuals who lived on minimum wage and in patients who had growth and developmental retardation ($p=0.001$, $p<0.001$). The hospitalization time was longer in these patients ($p=0.027$). The hemoglobin and sodium levels were significantly lower in patients who had extrapulmonary tuberculosis ($p=0.044$, $p=0.002$).

Öz

Amaç: Tüberküloz insanlık tarihinin en eski ve en bulaşıcı hastalıklarından birisidir. Dünya nüfusunun dörtte biri tüberküloz basili ile enfektedir. Çocukluk çağı tüberkülozunda standart bir klinik ve radyolojik tanımlama olmaması nedeniyle tanısı zordur. Bu çalışmada, kliniğimizde tüberküloz tanısı ile izlediğimiz çocuk olguların klinik, laboratuvar ve radyolojik bulgularını değerlendirilmiştir.

Gereç ve Yöntemler: Hastanemiz Çocuk Enfeksiyon Hastalıkları Servisi'nde Ocak 2015–Temmuz 2019 tarihleri arasında tüberküloz tanısıyla yatırılarak tedavi edilen 216 olgu geriye dönük olarak incelendi.

Bulgular: Olguların 129'u (%59,7) kız, 87'si (%40,3) erkekti. Hastaların yaş dağılımı 12,3 (0,33–18) yılı. Olguların 169'u (%78,2) akciğer tüberkülozu, 34'ü (%15,7) akciğer dışı tüberküloz tanılıydı, 13 hasta (%6) akciğer tüberkülozu ve akciğer dışı tüberküloz tanısı almıştı. Olguların 143'ünde (%66,2) tüberkülin deri testi pozitifliği vardı. Vücut sıvılarından alınan örneklerin 46'sında (%21,3) aside dirençli bakteri, 42'sinde (%19,4) kültürde *Mycobacterium tuberculosis* üremesi saptandı. Akciğer tüberkülozu ve akciğer dışı tüberküloz birlikteliği ailesi asgari ücretle geçinenlerde, büyüme gelişme geriliği olan hastalarda daha fazlaydı ($p=0,001$, $p<0,001$), bu hastaların yatış süreleri daha uzundu ($p=0,027$). Akciğer dışı tüberküloz hastalarının hemoglobin ve sodyum düzeyleri anlamlı olarak daha düşüktü ($p=0,044$, $p=0,002$).

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Cite this article as: Aygün D, Yıldırım T, Başoğlu Öner Ö, Şiraneci R. Evaluation of clinical and laboratory characteristics of childhood tuberculosis. *Turk Pediatri Ars* 2020; 55(3): 236–43.

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Received/Geliş Tarihi: 24.10.2019 **Accepted/Kabul Tarihi:** 20.03.2020

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DOI: 10.14744/TurkPediatriArs.2020.02438

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Conclusion: Although the diagnosis of childhood tuberculosis is difficult due to the nonspecific signs and symptoms, it is a preventable and treatable disease.

Keywords: Child, lung, tuberculosis

Çıkarımlar: Çocukluk çağı tüberkülozu özgül olmayan klinik belirti ve bulguları nedeniyle zor tanı alan bir hastalık olmakla birlikte önlenilebilir ve tedavi edilebilmektedir.

Anahtar sözcükler: Akciğer, çocuk, tüberküloz

Introduction

Tuberculosis (TB), which was discovered by Robert Koch in 1882, is one of the oldest diseases of humanity (1). A patient who died by producing bloody sputum along the Nile river was reported 3000 years before Christ, and *Mycobacterium tuberculosis* DNA was found in Egyptian mummies (2, 3). Tuberculosis still threatens human health today and ranks first among the infectious diseases leading to death caused by a single infectious agent worldwide. According to the World Health Organization (WHO) 2017 data, approximately 10 million people were diagnosed as having tuberculosis and 10% of these were pediatric patients (4). In the Turkey Tuberculosis Control 2018 report, the total TB incidence was reduced by 4.1% and the number of patients was reported as 12 417 (5). In regions where there is a high disease burden, children aged below 13 years constitute 13.7% of all TB cases (6). Childhood TB indicates that adulthood TB in the community is uncontrolled. The clinical characteristics of childhood TB differ from adults. The risk of lymphohematogeneous spread is high in children, and the risk of spread of infection and transformation to disease increases as the host's age decreases. The absence of a standard clinical and radiologic definition of TB in children causes diagnostic and therapeutic delays. In addition, rates of bacteriologic diagnosis are also low in children because clinical sampling techniques are difficult and the sensitivity of microbiologic tests is low in children (7–10). Epidemiologic data are limited in children because of the difficulties in the diagnosis of tuberculosis. Therefore, we aimed to evaluate the epidemiologic, clinical, and laboratory features of patients who were hospitalized in our clinic with a diagnosis of TB.

Material and Methods

Study plan

The data of all patients who were hospitalized in Kanuni Sultan Süleyman Education and Research Hospital, Pediatric Infectious Diseases Ward between January 2015 and July 2019 and diagnosed as having TB, were retrospectively examined from patient files and electronic recording systems. The patients' ages, sexes, heights and weight percentiles, underlying diseases and histories of Bacille Calmette-Guerin (BCG) vaccine were evaluated. A family history of TB and the presence of contact were investigated and the families' income levels were recorded according to minimum wage.

The patients' involvement sites, clinical symptoms, tuberculin skin test (TST) results, culture positivity, and laboratory and radiologic findings were evaluated. The diagnosis of TB was made with an interrogation of the family history of TB and history of contact, clinical symptoms, TST screening, lung radiography, computed tomography (CT), evaluation of body fluid samples, and growth in culture media.

Patient definition

The definitions and classifications of patients were made according to the Ministry of Health Tuberculosis Diagnosis and Treatment Guideline (11). Infection of the lung parenchyma or tracheal bronchial tree was named as pulmonary TB (PTB). If involvement of the lung parenchyma was absent, TB with pleural effusion or intrathoracic lymph node enlargement (hilar, mediastinal) was named as extra-pulmonary TB.

Patients in whom acid-resistant bacteria (ARB) could be demonstrated in samples obtained from organs other than lung parenchyma or patients with histologic and clinical findings compatible with TB were defined as having extrapulmonary TB (EPTB). Miliary TB was considered pulmonary and extrapulmonary TB.

Laboratory and radiologic evaluations

Fasting gastric juice, cerebrospinal fluid, urine, thoracentesis and paracentesis fluids and lymph node biopsy materials in cases with lymphadenopathy, were used for mycobacterial culture. The cultures were examined in Istanbul Yedikule Chest Diseases and Thoracic Surgery Education and Research Hospital Microbiology Laboratory and Istanbul University Istanbul Medical Faculty Department of Microbiology Laboratory. Löwenstein-Jensen media and Bactec media were used for culture examinations. The patients' samples were evaluated in terms of ARB positivity using Ehrlich-Ziehl-Neelsen (EZN) staining. At the time of diagnosis, hemogram, the mean erythrocyte sedimentation rate (ESR), mean C-reactive protein (CRP) values, vitamin D, serum electrolytes, albumin, and protein levels were evaluated before treatment in all patients.

The assessment of radiologic findings was based on the studies of our hospital's Division of Pediatric Radiology.

The patients were divided into three groups as pulmonary TB, extra-pulmonary TB, and the coexistence of both diagnoses, and their demographic findings, symptoms, and laboratory findings were evaluated. Approval was ob-

tained from our hospital's local ethics committee for the study (2019/04/100) and informed consent was obtained from the parents of all patients. The study was conducted in accordance with the Helsinki Declaration.

Statistical Analysis

Statistical analysis was performed using the IBM SPSS Statistics software (Windows Sürüm 21.0. Armonk, NY: IBM Corp.). Continuous variables are presented as median (range) and categorical variables are presented as frequency (as percentage). Qualitative values were compared using Pearson's Chi-square and Fisher's exact tests (as some results were 1 and even 0) between the groups. As the sample size of our study was larger than 30, the normality of distribution of continuous data was tested using the Kolmogorov-Smirnov test. The significance value was <0.05 for most of the demographic and prognostic factors in this test. Therefore, Kruskal-Wallis, which was a non-parametric test, was used in the comparison of subjects with TB by diagnosis. A p-value of <0.05 was considered statistically significant for all tests.

Results

The subjects' characteristics and distribution

One hundred twenty-nine (59.7%) of 216 patients with a diagnosis of TB were female and 87 (40.3%) were male. The median age was found as 12.3 (range, 0.33–18) years. One hundred sixty-nine (78.2%) of the subjects were diagnosed as having pulmonary TB and 34 (15.7%) had extra-pulmonary TB. Among the subjects who were diagnosed as having extra-pulmonary TB, 13 (38.2%) had lymph node TB, six (17.6%) had gastrointestinal TB, six (17.6%) had miliary TB, five (14.7%) had pleural TB, four (11.7%) had intrathoracic lymph node TB, three (8.8%) had TB meningitis, one (2.9%) had bone TB, one (2.9%) had pericardial TB, and one (2.9%) had renal TB. Histopathologic evaluations were performed in all subjects who had lymph node TB and gastrointestinal TB.

When the distribution of the subjects by years was examined, it was found that 18 (8.3%) patients were hospitalized in 2019, 30 (13.9%) were hospitalized in 2018, 55 (25.5%) were hospitalized in 2017, 44 (20.4%) were hospitalized in 2016, and 69 (31.9%) patients were hospitalized in 2015. One hundred two (47.2%) subjects had a bodyweight below the 3rd percentile. The families of 126 (58.3%) subjects were living on minimum wage. Ten (4.6%) patients had an underlying disease, four (1.8%) had juvenile idiopathic arthritis, two (0.9%) had nephrotic syndrome, one (0.4%) had hyperimmunoglobulin D, one (0.4%) had hereditary spherocytosis, and one (0.4%) patient had chronic granulomatous disease. Bacille-Calmette-Guerin (BCG) vac-

cine was administered to 172 (79.6%) of the subjects. One hundred thirty-six (63%) patients had a history of contact. Contact with a father who had TB was found in 60% of the subjects. Although a drug sensitivity test was not performed in all index cases, multi-drug resistant tuberculosis (MDR-TB) was found in six of the index cases.

The most common symptoms at presentation was cough (n=177, 81.9%). The other symptoms at presentation included fever (n=159, 73.6%), weight loss (n=71, 32.9%), night sweats (n=35, 16.2%), sputum production (n=33, 15.2%), hemoptysis (n=26, 12%), and erythema nodosum (n=3, 1.3%).

TST positivity was found in 143 (66.2%) subjects. Pathologic findings were found on lung radiography in 180 (83.3%) of the subjects and on thoracic computed tomography (CT) in 182 (84.2%). When the radiologic findings were evaluated, hilar and/or mediastinal lymph nodes were found in 158 (73.1%) subjects, patchy or lobular consolidation areas were found in 124 (57.4%) subjects, branching linear and nodular opacities defined as budded tree mark were found in 60 (27.8%) subjects, cavitation was found in 43 (19.9%) subjects, lobar consolidation was found in 27 (12.5%) subjects, and pleural effusion was found in 19 (8.8%) subjects.

ARB and Mycobacterium tuberculosis polymerase chain reaction (PCR) were found to be positive in 46 (21.3%) of fasting gastric juice samples or the samples obtained from body fluids, and Mycobacterium tuberculosis growth was positive in 42 (19.4%). Isoniazid resistance was found in three (1.3%) samples and MDR-TB was found in nine (4.1%). The patients' demographic characteristics are shown in Table 1.

On complete blood count evaluation, the median ESR was found AS 35.8 (range, 1–134) mm/h, the median CRP was found as 11.56 (range, 0.08–208) mg/L, the median white blood cells (WBC) was 9050 (range, 1850–29 170)/mm³, the median neutrophil count was found as 4900 (range, 100–24 900)/mm³, the median lymphocyte count was 2500 (range, 300–14 100)/mm³, the median platelet count was found as 358 000 (range, 87 870–964 800)/mm³ and the median hemoglobin level was found as 11.6 (range, 7.18–15.4) g/dL.

Biochemical evaluation revealed that the median calcium level was 9.5 (range, 7–13) mg/dL, the median phosphorus level was 4.5 (range, 2.2–6.2) mg/dL, the median magnesium level was 2 (range, 1.2–8) mg/dL, the median sodium level was 138.5 (range, 129–149) mmol/L, the median potassium level was 4.5 (range, 2.3–5.6) mmol/L, the median albumin level was 4.2 (range, 1.7–5.3) g/L, and the median protein level was 7.3 (range, 4.4–10.1) g/L.

Table 1. Demographic properties of the patients

Total number of patients	n=216	
	n	%
Diagnosis		
Pulmonary TB	169	78.2
Extrapulmonary TB	34	15.7
Pulmonary and extrapulmonary TB	13	6
Sex		
Male	87	40.3
Female	129	59.7
Age distribution of the patients (years) median (minimum-maximum)	12.3 (0.33–18)	
Familial history	136	63
BCG vaccine	172	79.6
Living on minimum wage	126	58.2
Growth and developmental retardation	102	47.2
Complaint		
Cough	177	81.9
Fever	159	73.6
Weight loss	71	32.9
Night sweats	35	16.2
Sputum production	33	15.2
Hemoptysis	26	12
Erythema nodosum	3	1.3
TST positivity	143	66.2
Histopathologic diagnosis	19	8.8
Comorbidity	10	4.6
Presence of acid-resistant bacteria	46	21.3
Mycobacterium tuberculosis DNA	46	21.3
Growth in culture	42	19.4
Multi-drug resistant TB	9	4.1

BCG: Bacillus Calmette Guerin; DNA: Deoxyribonucleic acid; TB: Tuberculosis; TST: Tuberculin skin test

The median vitamin D level was found as 9.47 (range, 2–42) ng/mL in our subjects. A vitamin D level of <12 ng/mL was considered deficiency, a level of 12–20 ng/mL was considered insufficiency, and a level of >20 ng/mL was considered normal. Vitamin D deficiency was found in 62% of the subjects, vitamin D insufficiency was found in 29.2%, and normal vitamin D levels were found in only 8.8%.

When the cases of TB were divided into three groups as PTB, EPTB, and PTB+EPTB, and were compared between each other, the association of PTB and EPTB was found with a higher rate in families who lived on the minimum wage and in patients who had growth and developmental retardation ($p=0.001$, $p<0.001$). In addition, the hospi-

talization time was longer in patients who had an association of PTB and EPTB ($p=0.027$). When the subjects' blood count and laboratory values were compared, it was found that the hemoglobin and sodium values were significantly lower in patients with EPTB ($p=0.044$, $p=0.002$) and no significant difference was observed in the other laboratory values. Comparison according to the localization of the TB is shown in Table 2.

The mean hospitalization time was found as 23.02 ± 16.5 days in our subjects. Quartet treatment involving isoniazid, rifampicin, pyrazinamide and ethambutol, was initiated in our subjects. Ophthalmologic examinations were performed in all subjects before ethambutol treatment and visual impairment developed in one patient who had a diagnosis of MDR-TB. No visual problems occurred in the other subjects. During treatment, a transient elevation in liver enzymes developed in 10 (4.6%) patients and elevation in uric acid levels developed in seven (3.2%) patients as drug adverse effects; discontinuation of treatment was not needed. Two patients received mechanical ventilator support because of respiratory distress and no patient was lost. In our subjects who had multi-drug resistant TB and who were ARB positive, follow-up samples were obtained 3–6 weeks after treatment initiation, and smears were found to be negative.

Discussion

In our study, the clinical, laboratory, and radiologic findings of 216 children who were diagnosed as having TB, hospitalized, and treated, were evaluated. Our youngest subject was aged 4 months and the median age of our patients was 12.3 (range, 0.33–18) years. Throughout our country, the total number of subjects aged between 0 and 17 years is 1090; 630 patients (57.8%) have been reported in the 0–14-year age group, and 460 (42%) patients have been reported in the 15–17-year age group (5). In parallel to the general data, the distribution of our subjects by age groups was as follows: 134 patients (62%) were aged between 0 and 14 years and 82 patients (38%) were aged 15–17 years. It is known that the risk of transformation of TB infection to disease and the development of serious disseminated disease increases, especially with younger age in children. However, no significant difference was found in terms of TB dissemination when we compared our patients by age groups.

Although the tuberculosis bacillus frequently tends to cause disease in the lung, it may involve all tissues and organs without making organ discrimination (12). In our country, pulmonary involvement has been reported with a rate of 61.3%, extra-pulmonary involvement has been reported with a rate of 33.6%, and the association of both

Table 2. Comparison of tuberculosis cases by diagnosis

	Pulmonary TB (n=169)	Extrapulmonary TB (n=34)	Association of PTB and EPTB (n=13)	p
	Median (Min.–Max.)	Median (Min.–Max.)	Median (Min.–Max.)	
Sex (male)	64 (37.8%)	14 (41.1%)	9 (69.2%)	0.084
Age (years)	12.5 (0.33–18.0)	11.4 (0.6–16.8)	14.3 (3.5–17.6)	0.526
Minimum wage	89 (52.6%)	24 (70.5%)	13 (100%)	0.001
Growth and developmental retardation	68 (40.2%)	21 (61.7%)	13 (100%)	<0.001
Contact	115 (68.0%)	17 (50%)	4 (30.7%)	0.006
Fever	129 (76.3%)	20 (58.8%)	10 (76.9%)	0.103
Weight loss	51 (30.1%)	13 (38.2%)	7 (53.8%)	0.168
Night sweat	28 (16.5%)	5 (14.7%)	2 (15.3%)	0.957
TST positivity	112 (66.2%)	22 (64.7%)	9 (69.2%)	0.958
ARB positivity	37 (21.8%)	6 (17.6%)	3 (23%)	0.848
PCR positivity	37 (21.8%)	6 (17.6%)	3 (23%)	0.848
Cultur positivity	34 (20.1%)	5 (14.7%)	3 (23%)	0.725
Drug resistance	11 (6.5%)	0 (0%)	1 (7.6%)	0.302
Hospitalization time	18.0 (2–114)	18.5 (5–100)	34 (6–60)	0.027
Sedimentation rate (mm/h)	34 (4–116)	39.5 (4–134)	36 (1–121)	0.794
C-reactive protein (mg/L)	11.6 (0.08–139.8)	12.3 (0.87–208)	10.5 (2.3–92.9)	0.719
WBC (/mm ³)	9150 (1850–29 170)	8240 (5 050–16 110)	8970 (4660–17 410)	0.306
Neutrophil count (/mm ³)	5110 (100–2 490)	4145 (1 200–13 400)	5800 (2050–12 900)	0.048
Lymphocyte count (/mm ³)	2500 (300–14 100)	2800 (700–7 900)	2600 (1300–5500)	0.926
Platelet count (/mm ³)	358 000 (87 870–964 800)	378 600 (183 000–832 000)	327 200 (205 000–462 400)	0.580
Hemoglobin (g/dL)	11.6 (7.2–15.4)	11.1 (7.9–14.2)	11.1 (8.6–14.8)	0.044
Vitamin D (ng/mL)	9.6 (2–34.6)	9.5 (3–42)	9.2 (3–25.2)	0.780
Calcium (mg/dL)	9.5 (7.2–11.2)	9.6 (7.7–10.6)	8.9 (7–13)	0.361
Phosphorus (mg/dL)	4.4 (2.3–6.2)	4.9 (2.2–6)	4.2 (2.5–5.1)	0.034
Magnesium (mg/dL)	2 (1.2–8)	2 (1.3–2.3)	2 (1.54–2.6)	0.271
Sodium (mmol/L)	139 (131–145)	137 (130–141)	138 (129–149)	0.002
Potassium (mmol/L)	4.5 (3.5–5.2)	4.5 (2.3–5.6)	4.4 (2.9–5.3)	0.702
Albumin (g/L)	4.2 (1.7–4.6)	4.2 (2.3–4.7)	3.8 (1.8–4.4)	0.032
Protein (g/L)	7.4 (4.4–10.1)	7.4 (6–10.8)	7.1 (4.6–8.4)	0.202

ARB: Acid-resistant bacillus; PCR: Polymerase chain reaction; WBC: White blood cell; TB: Tuberculosis; TST: Tuberculin skin test; Min.: Minimum; Max.: Maximum

pulmonary and extra-pulmonary involvement has been reported with a rate of 5.1% (5). In children, mostly pulmonary parenchymal involvement and intrathoracic involvement is observed. A diagnosis of pulmonary TB was made in 78.2% of our subjects. As the risk of lymphohematogenous dissemination is greater in children, EPTB is observed more frequently compared with adults. However, EPTB is generally underreported, because the clinical findings of EPTB are extremely variable and nonspecific, and immunologic and microbiologic tests have low sensitivity. In different studies, the rates of EPTB in children

range between 24.8% and 47.4% (13, 14). The rate of EPTB was found as 33.8% in children in a study from our country, whereas it was 19.6% in a study conducted by Turel et al. (15); EPTB was diagnosed in 15.7% of our subjects. Lymphadenitis is the most common form of EPTB (16). In our study, the most common finding of EPTB was found as lymphadenitis and the other EPTB forms included milary TB and gastrointestinal TB.

The relationship of TB with nutrition is well known. In ancient Greece, the disease was called 'phtthisis,' because

patients died due to losing weight. The fact that the disease is observed more frequently in societies with poor socioeconomic conditions, supports inadequate nutrition (17, 18). Although the cause of weight loss is not clear, it has been proposed that excessive release of inflammatory cytokines including interferon (IFN)- γ , interleukin (IL)-10, and tumor necrosis factor (TNF)- α , may be involved. The weight in 47.2% of our subjects was below the 3rd percentile and the families of 58.2% lived on minimum wage. The association of PTB and EPTB was found with a higher rate in subjects who lived on minimum wage and in patients who had growth and developmental retardation.

The diagnosis of TB in children is based on evaluation of familial and contact history, TST or IFN- γ release assay (IGRA) results, clinical findings, and radiologic and microbiologic findings (19). The interrogation of a history of contact with an adult who has active TB is important in making the diagnosis. The risk of disease increases in the presence of long-term and close contact, such as in-house contact. A history of contact was present in 63% of our patients and in-house contact was found with a high rate. Rates of contact have been reported as 25–64% (20, 21). The WHO recommends that all children aged between 0 and 4 years and symptomatic children aged over 5 years should be evaluated in terms of TB if a history of contact is present (22). Knowing ARB positivity and evaluation of culture results in subjects with a history of contact is also important in terms of early diagnosis in cases of MDR-TB. MDR-TB was found in six of our index cases. No significant association was found between the presence of contact and PTB and EPTB.

Although the tuberculin skin test is the main test is used in TB screening, the fact that it is influenced by many factors such as BCG vaccine, individual immunity, and application and interpretation technique, causes low sensitivity and specificity. By contrast, the sensitivity and specificity of IGRAs are very high. Although there are data indicating the superiority of IFN- γ release assays in the diagnosis, the WHO recommends not to prefer IGRA over TST in the diagnosis of TB in moderate and low-income countries (23). Both tests are positive in both latent TB infection and TB disease and their diagnostic value is limited (11). In our study, IGRA could not be evaluated because IGRA could not be performed in all our subjects due to the high cost. TST was found positive in 66.2% of our subjects and there was no significant difference between PTB and EPTB in terms of TST positivity.

In childhood TB, clinical signs and symptoms are not specific and may mimic many diseases. In our subjects with pulmonary TB, the most common symptom was cough,

and the others included fever, weight loss, and night sweats. Although there are data reporting that constitutional symptoms such as fever, weight loss, and malaise are observed with a lower rate in EPTB, no significant difference was found between PTB and EPTB in terms of clinical symptoms in our study (24).

In TB, anemia, thrombocytopenia, and hypoalbuminemia, which are among the findings of chronic inflammation, may be observed, and acute-phase reactants may be increased. Increased ESR and CRP were found in 44% of our subjects, leukocytosis was found in 20.4%, and anemia was found in 48%. Anemia was found with a higher rate in the subjects who had EPTB.

It has been known for many years that vitamin D influences the immune response to TB and provides protection against TB by way of its actions on the immune system via various mechanisms. 1,25-hydroxyvitamin D₃ decreases the vitality of *Mycobacterium tuberculosis* by increasing the fusion of phagosomes and lysosomes in infected macrophages (25). Vitamin D deficiency is associated with increased TB risk in different populations. Vitamin D levels were found to be low in the majority of our subjects; only 8.8% of our subjects had normal vitamin D levels. No significant difference was found between the TB subgroups in terms of vitamin D, calcium, phosphorus, and magnesium levels.

Inappropriate antidiuretic hormone release and hyponatremia may be observed in cases of TB. Serum sodium levels were found to be below 135 mEq/L in 13% of our subjects and significantly low in patients who had EPTB.

Radiologic evaluation is very important in the diagnosis of TB. Although lung radiography is the most commonly used method, its sensitivity is 70–80% and specificity is 60–70% in the diagnosis of TB (11). Computed tomography is more sensitive for the evaluation of parenchymal infiltrations, ground-glass opacities, cavities, mediastinum, hilus, and structures adjacent to the pleura. Kamer et al. (26) from Turkey observed no findings in lung radiography in favour of TB in 38% of patients who were diagnosed as having pulmonary TB using CT. Boloursaz et al. (27) reported that lung radiography was normal in 31% of patients who were diagnosed as having pulmonary TB. In the majority of our study group, lung radiography and CT findings were evaluated in association and the most common radiologic finding was found as hilar and/or mediastinal lymph nodes (27). Cavitory TB was found with a high rate (19.9%) when compared with the literature. Although it has been reported that lymph node involvement is more frequent and parenchymal involve-

ment is less frequent in children aged below three years compared with older children, we found no significant difference in radiologic findings by age in our study (27).

Demonstrating the bacillus is not always possible in childhood TB. In children, bacteriologic diagnosis rates are low because clinical sampling techniques are difficult and the sensitivity of microbiologic tests is low. Many studies have shown a culture positivity ranging between 0% and 40% (28, 29). ARB and PCR were found to be positive in 21.3% of our subjects, and culture positivity was found in 19.4%. Isoniazid resistance was found with a rate of 1.3% and MDR-TB was found with a rate of 4.1%. Resistance to isoniazid and rifampicin, which are the most important drugs in the treatment of TB, is called MDR-TB. Çakır et al. (30) found MDR-TB with a rate of 8% in children. Drugs used in the treatment of TB are generally in the form of tablets prepared for adults, but children can tolerate high doses better and the rates of adverse effects are low. The rate of drug adverse effects was 8.3% in our subjects.

The limitations of our study included the retrospective design and the fact that our microbiologic results were relatively few. The strong aspects of our study included the high number of patients and the fact that the blood counts and laboratory findings of our patients were also evaluated.

In conclusion, the diagnosis of TB in childhood is based on the evaluation of the symptoms, history of contact, TST positivity, and clinical, radiologic, and microbiologic findings in association. In our study, the clinical and laboratory findings of pediatric patients with TB were evaluated. The association of PTB and EPTB was found with a higher rate in families who lived on minimum wage and in patients with growth and developmental retardation, and the hospitalization time was longer in these patients. Hemoglobin and sodium levels were significantly lower in patients with extrapulmonary TB. All our patients were treated successfully. No patient was lost and no disease recurrence occurred during the study.

Ethics Committee Approval: Approval was obtained from the local ethics committee of our hospital for the study (2019/04/100).

Informed Consent: Consent was obtained from the parents of all patients.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - D.A., R.Ş.; Design - D.A.; Supervision - R.Ş.; Funding - T.Y., Ö.B.Ö.; Materials - T.Y.;

Data Collection and/or Processing - D.A.; Analysis and/or Interpretation - D.A.; Literature Review - D.A.; Writing - D.A.; Critical Review - R.Ş., T.Y., Ö.B.Ö.

Conflict of Interest: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Etik Kurul Onayı: Çalışmamız için hastanemiz lokal etik kurulundan onay alındı (2019/04/100).

Hasta Onamı: Tüm hastalarımızın ebeveynlerinden onay alınmıştır.

Hakem Değerlendirmesi: Dış bağımsız.

Yazar Katkıları: Fikir - D.A., R.Ş.; Tasarım - D.A.; Denetleme - R.Ş.; Kaynaklar - T.Y., Ö.B.Ö.; Malzemeler - T.Y.; Veri Toplanması ve/veya İşlemesi - D.A.; Analiz ve/veya Yorum - D.A.; Literatür Taraması - D.A.; Yazıyı Yazan - D.A.; Eleştirel İnceleme - R.Ş., T.Y., Ö.B.Ö.

Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Mali Destek: Yazarlar bu çalışma için mali destek almadıklarını beyan etmişlerdir.

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