Cukurova Medical Journal
ÇUKUROVA ÜNİVERSİTESİ TIP FAKÜLTESİ

Cukurova Med J 2020;45(4):1698-1706
DOI: 10.17826/cumj.780991

ARAŞTIRMA / RESEARCH

Epidemiologic features and treatment outcomes of pediatric pulmonary tuberculosis cases

Pediatrik pulmoner tüberküloz olgularının epidemiyolojik özellikleri ve tedavi sonuçları

Pınar Etiz[1], Ali Tanju Altunsu[2]

[1] Cukurova University, Abdi Sütçü Vocational School of Health Services, Adana, Turkey
[2]Adana Provincial Directorate of Health, Head of Public Health Services, Adana, Turkey

Cukurova Medical Journal 2020;45 (4):.1698-1706

Abstract

Purpose: Pediatric tuberculosis constitutes a significant part of the global burden of tuberculosis. It is also important in that it shows that the burden of tuberculosis continues in society. We here aimed to examine the epidemiologic features and treatment outcomes of pediatric pulmonary tuberculosis cases who were registered to the Adana Tuberculosis Dispensaries.

Material and Methods: Fifty-six pediatric patients aged 0-18 years with the diagnosis of pulmonary tuberculosis were examined retrospectively in terms of demographic data, clinical characteristics and drug susceptibility test results, as well as treatment outcomes. Data were collected through medical record review.

Results: The mean age of the patients was 12.84 ± 5.62 years and 46.4% were female. Nine patients (16%) were aged 0-5 years, 4 (7.1%) were aged 5-10 years, 17 (30.3%) were aged 10-15 years and 26 patients (46.4%) were aged 15-18 years. Fourty-eight children was only pulmonary tuberculosis whereas eight possessed characteristics of both pulmonary and extrapulmonary tuberculosis. The most frequent symptoms were prolonged cough (80.3%) and weight loss (73.2%). Drug susceptibility test was performed only 22 patients. Multidrug resistance was determined in one patient. Among the 56 children for whom treatment outcome was documented, 39 (69.6%) were completed treatment, 16 (28.5%) were cured and 1 (1.7%) had treatment failure.

Conclusion: It was observed that the signs and symptoms of our patients were compatible with the literature. The epidemiological characterization of pediatric patients with pulmonary tuberculosis helps to provide a better diagnostic approach in this population.

Keywords:. Mycobacterium tuberculosis, pediatrics, public health, pulmonary tuberculosis

Öz

Amaç: Pediatrik tüberküloz dünya çapında tüberküloz yükünün önemli bir kısmını oluşturmaktadır. Pediatrik tüberküloz toplumda tüberküloz yükünün devam ettiğini göstermesi bakımından da önemlidir. Çalışmamızda Adana ili Tüberküloz Dispanserlerine kayıtlı olan pediatrik pulmoner tüberküloz olgularının epidemiyolojik özelliklerini ve tedavi sonuçlarını incelemeyi amaçladık.

Gereç ve Yöntem: Pulmoner tüberküloz tanısı konan 0-18 yaş arası 56 çocuk demografik veriler, klinik özellikler, ilaç duyarlılık testi ve tedavi sonuçları açısından geriye dönük olarak incelenmiştir. Veriler tıbbi kayıtlardan elde edilmiştir.

Bulgular: Yaş ortalaması 12,84 ± 5,62 olan olguların %46,4'ü kız idi. Sıfır-5 yaş arası 9 olgu (%16), 5-10 yaş arası 4 olgu (%7,1), 10-15 yaş arası 17 olgu (%30,3), 15-18 yaş arası 26 olgu (%46,4) vardı. Kırk sekiz çocukta sadece akciğer, sekizinde hem akciğer hem de akciğer dışı tutulum vardı. En sık görülen semptomlar uzun süren öksürük (%80,3) ve kilo kaybı (%73,2) idi. Sadece 22 hastaya ilaç duyarlılık testi uygulandı. Bir hastada çoklu ilaç direnci belirlendi. Tedavi sonuçları incelenen 56 çocuktan 39'u (%69,6) tedavisini tamamladı, 16'sında (%28,5) kür ve 1'inde (%1,7) tedavi başarısızlığı olduğu kaydedildi.

Sonuç: Hastalarımızın belirti ve bulgularının literatür ile uyumlu olduğu gözlendi. Pediatrik pulmoner tüberküloz olgularının

Anahtar kelimeler: Halk sağlığı, pediatri, pulmoner tüberküloz, Mycobacterium tuberculosis

Yazışma Adresi/Address for Correspondence: Dr. Pınar Etiz, Cukurova University, Abdi Sutcu Vocational School of Health Services, Adana, Turkey E-Mail: pinaretiz@yahoo.com
Geliş tarihi/Received: 15.08.2020 Kabul tarihi/Accepted: 10.10.2020 Published online:

INTRODUCTION

Pulmonary tuberculosis is a common lung infection globally and has a higher prevalence in developing countries. It has become a main social and medical problem with high mortality and morbidity. The World Health Organization (WHO) publishes global tuberculosis data including new and relapse cases by age. In the 2018 report, the WHO estimates that of the estimated 10 million incident cases of tuberculosis in 2017, approximately 1 million (10 percent) occurred among children <15 years; similar numbers of boys and girls were affected. In 2018, the WHO estimated that there were 234,000 deaths owing to tuberculosis in children <15 years (40,000 occurring in HIV-infected children). These deaths represent 15 percent of all tuberculosis deaths (which is higher than the estimated proportion of cases in children), suggesting a higher mortality rate in this age group[1]. This burden emphasizes the requirement to overcome the barriers to combatting tuberculosis in children which is recognized as one of the leading causes of death in this age group[2]. The most of children who suffer from tuberculosis disease present pulmonary manifestations, but 25 to 35 % of children possess an extrapulmonary sign[3]. Childhood tuberculosis reflects uncontrolled adult tuberculosis in a community[4]. Therefore, the identification and effective treatment of children with tuberculosis in the community is an important point in the fight against tuberculosis[5]. The progress and clinical findings of tuberculosis developing in children differ from those in adults since children possess fewer positive mycobacterial cultures and less specific findings and symptoms than adults. Hence, the diagnosis of tuberculosis is difficult and its presence is seldom demonstrated[6]. In childhood, there are problems in microbiological confirmation of tuberculosis diagnosis because of low bacillus load or the patients' inability to provide adequate sputum specimens[5]. The microbiological confirmation rate is low, and initial criteria for the diagnosis of tuberculosis is generally established employing a combination of history, chest radiograph data and tuberculin skin test (TST) positivity[4]. Even though pediatric tuberculosis still has a public health emergency, there are limited data on research and surveillance. Strong regional data are needed to define the impact of the disease and for timely detection[7]. The data of pediatric patients with pulmonary tuberculosis presented in this research, helps to achieve a better diagnostic approach in this population.

There are limited data on the incidence and clinical course of pediatric tuberculosis, which are mostly reported from low-burden countries[6]. This situation has recently sparked the researcher's interest since children represent 15 to 20% of all tuberculosis cases, which may increase up to 40% in countries where the disease is endemically seen[8]. Over the years, several studies have been performed on the burden, diagnosis, and treatment outcomes of tuberculosis seen during childhood. Many tuberculosis cases in adults have been reported from Turkey. However, there are limited tuberculosis cases in children to do planning for this age group[2]. Data are needed to define the impact of the disease and to strengthen measures for detection and treatment.

This study aimed to fill this gap and assess the demographic, diagnostic strategies and clinical characteristics, as well as treatment outcomes among children diagnosed with pulmonary tuberculosis from Adana, Turkey.

MATERIAL AND METHODS

The study was conducted in accordance with the principles of the Declaration of Helsinki. Ethics committee approval was received for this study from the ethics committee of Cukurova University School of Medicine (document no: 2018/82/36, date: 02.10.2018)

Procedure

The medical records of pediatric patients under the age of 18 years, who were diagnosed with pulmonary tuberculosis, and treated with an anti-tuberculosis regimen, were collected from tuberculosis dispensaries in the province of Adana from January 1, 2014 to December 31, 2017, retrospectively. There are 4 tuberculosis dispensaries in Adana province. These patients' records were examined considering demographic data (age, gender, country of birth (Turkey or other country), tuberculosis exposure, Bacille Calmette-Guérin (BCG) vaccination status), clinical features (history of previous tuberculosis episodes, signs or symptoms of tuberculosis), microbiological results of biological samples (smear and/or culture results), drug susceptibility test results and responce to treatment[7,9-11]. Patients followed in

another center after starting treatment were omitted from the study.

History of Contact: Household contact is defined as a person sharing the same closed living space as the index case for one or more nights or for frequent or extended daytime periods during the three months prior to starting the current treatment regime. An investigation of source case is performed to recognize an infectious person who could be the source case of someone with tuberculosis or latent infection with *Mycobacterium tuberculosis* (*M. tuberculosis*)[4].

Anatomical Site of the Disease: Pulmonary tuberculosis describes as any bacteriologically confirmed or clinically diagnosed case of tuberculosis involving the pulmonary parenchyma or the tracheobronchial tree[4]. Cases who have clinical findings belonging to organs other than lung parenchyma and are diagnosed with tuberculosis radiologically, microbiologically and histo-pathologically are identified as extrapulmonary tuberculosis[5]. Both pulmonary and extrapulmonary tuberculosis cases are classified as a case of pulmonary tuberculosis[4,7].

Diagnostic Criteria: Microbiological tests contained direct microscopy by Erlich Ziehl-Nielsen stain for the presence of Acid-Resistant Bacilli (ARB) and *M. tuberculosis* culture in Mycobacteria Growth Indicator Tube/Lowenstein-Jensen medium of clinical samples including sputum, gastric lavage and bronchoalveolar lavage. In case that the child was able to produce sputum or gastric lavage could be done, samples were submitted to smear microscopy for ARB. Children with positive smear outcomes were characterized as smear-positive tuberculosis. Those with negative smear results were classified as smear negative tuberculosis if the child had tuberculosis after a further clinician's evaluation by means of a thorough clinical assessment and chest radiography[2]. Children receiving a clinical diagnosis of tuberculosis were those not be able to produce sputum or in whom gastric lavage could not be performed and microscopic examination and/or culture was not performed for sputum but had physical signs, chest radiography suggestive of pulmonary tuberculosis and a history of contact with a tuberculous person and were evaluated by a clinician whether to develop tuberculosis[2,4,7,9-11]. For assessment based on previous anti-tuberculosis treatment, patients were classified as a new patient and previously treated patient[7]. New patients had either received treatment for anti-tuberculosis or tuberculosis medicines for less than one month. Previous treatment history was categorised as relapsed patients (a patient previously treated for tuberculosis who had been declared cured or treatment completed and were currently diagnosed with positive smear or culture), interrupted treatment (a patient who returns for treatment, positive bacteriologically, following interruption of treatment for two months or more), and treatment failure (a patient who is started on re-treatment regimen after failing previous treatment, i.e., having a positive bacteriological result at month 5 of treatment)[12].

Treatment Outcome Definitions

Treatment results are reported with a similar terminology in all countries of the world. The treatment outcome was divided into six categories recommended by the world health organization used in our country is listed below. These categories were as follows[13,14]:

a. Cured: Finishing treatment with negative bacteriology result at the end of treatment.
b. Treatment completed: Finishing treatment but without bacteriology result at the end of treatment.
   Successfully treated: A combination of cure and treatment completed.
c. Died: Patients who died from any cause during the course of treatment
d. Treatment failure: Remaining smear positive at five months despite correct intake of medication.
e. Lost to follow-up: Patients who interrupted their treatment for two consecutive months or more after registration.
f. Transfer-out: Patients whose treatment results are unknown due to transfer to another health facility.

Statistical Analysis

The Statistical Package for the Social Science (SPSS) statistical program was used for data analyses (Version 21 for windows, Chicago, IL, USA). All records pertaining to pediatric pulmonary tuberculosis cases diagnosed during the study period were collected and analysed. Descriptive statistics were conducted for demographic and clinical variables including gender, age, country of birth, category of patients, site of disease and microbiological results. The association between the independent variables and treatment outcomes were assessed using Chi-square test. A p-value less than 0.05 was considered to be significant.

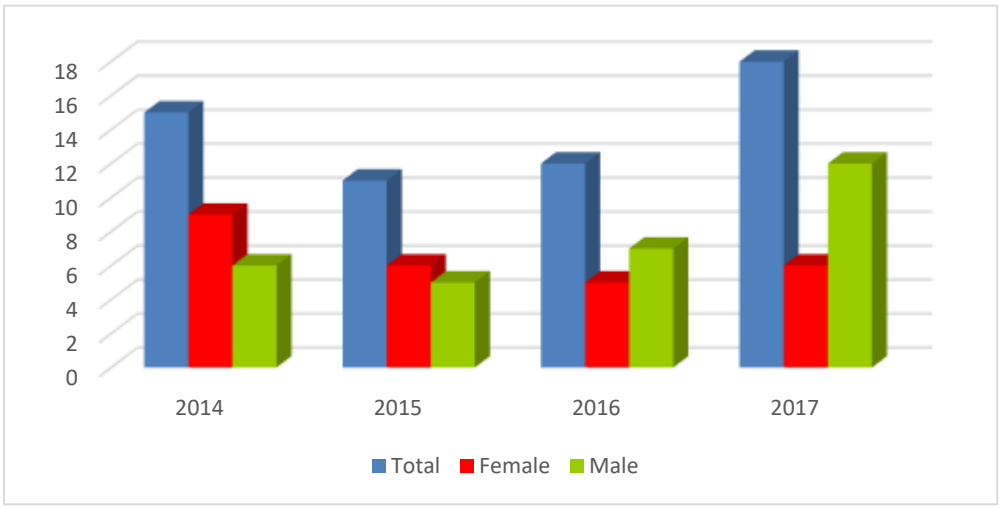

Figure 1. Distribution of children diagnosed with pulmonary tuberculosis by year and sex, 2014 – 2017.

Table 1. General demographic characteristics of pediatric pulmonary tuberculosis cases, 2014-2017

Variable	N (%)
Sex	
Female	26 (46.4%)
Male	30 (53.5%)
Age at diagnosis (years)	
0-5	9 (16%)
5-10	4 (7.1%)
10-15	17 (30.3%)
15-18	26 (46.4%)
Country of birth	
Turkey	46 (82.1%)
Other Country	10 (17.8%)
Category of patients	
New	52 (92.8%)
Relaps	3 (5.3%)
Defaulter	1 (1.7%)
Site of disease	
Pulmonary	48 (85.7%)
Pulmonary+Extrapulmonary	8 (14.2%)
BCG Vaccination Status	
Yes	29 (51.7%)
No	27 (48.2%)
Contact history of a tuberculosis patient	
Yes	20 (35.7%)
No	36 (64.2%)

RESULTS

During the study, 56 children were diagnosed with pulmonary tuberculosis; of which them 48 (85.7%) had only pulmonary and 8 cases (14.2%) had both pulmonary and extrapulmonary involvement. Of the 56 children who were included in the study, 30 (53.5%) were male and 26 (46.4%) were female. The mean age was 12.84 ± 5.62 ranging between 0 and 18 years with the highest prevalence among the 15-18 years of age group (46.4%). Fortysix of the patients are Turkish citizens and 10 of them are foreign nationals (Syria). Fiftytwo patients (92.8%) were classified as new patient, three patients (5.3%) were classified as relapse patient and one patient (1.7%) as a defaulter. There was no significant relationship was observed in this study population between treatment outcome and gender, country of birth and category of patients ($p>0.05$). Table 1 shows the demographic characteristics of the study population. More children (32.1%) were diagnosed in 2017 compared to the other years as shown in fig.1. Based on reports, 20 (35.7%) of the patients diagnosed with pulmonary tuberculosis, there was a history of household contact with an adult with active tuberculosis, 36 (64.2%) had no history of contact. An infectious person who might be the source case was identified for 13 patients: Five fathers, two mothers, one siblings, and three grandfathers/grandmothers and two multiple contacts. Identified source cases are shown in table 2. There was no significant association between treatment outcome and contact history ($p>0,05$). In 29 (51.7%) of patients had the BCG vaccine BCG scars (62% had 1 scar and 37.9% had at least 2 scars). Twenty-seven patients did not have any BCG scars. There was no significant relationship was observed in our study population between treatment outcomes and BCG vaccination status ($p>0.05$). Prolonged cough persisting for more than 2 weeks (80.3%) and weight loss (73.2%) were the most common symptoms. Clinical symptoms of children with pulmonary tuberculosis as shown in Table 3.

Microbiological evaluation (direct microscopy and/or culture) was available for 43 (76.7%, 43/56) patients. ARB was analyzed 43 of the patients with pulmonary tuberculosis diagnosis and it was positive in 23 (53.4%, 23/43). *M. tuberculosis* culture was sent from 39 (90.6%, 39/43) of the patients diagnosed with pulmonary tuberculosis. *M. tuberculosis* growth was detected in a total of 24 (61.5%, 24/39) patients. Among 38 children who had both smear microscopy and culture performed, 17 (44.7%) had a positive result. Sputum was the most commonly studied specimen for identifying tuberculosis bacilli.

Table 2. Index cases identified

Index Case	Number
Mother	2
Father	5
Sibling	1
Grandmother	1
Grandfather	2
Multiple contacts*	2

* Both parents 1, Sibling and father 1.

Table 3. Clinical features of children with pulmonary tuberculosis

Symptoms	Number (%)
Cough	45 (80.3%)
Sputum extraction	23 (41.0%)
Weakness	27 (48.2%)
Weight loss	41 (73.2%)
Night sweating	29 (51.7%)
Fever	21 (37.5%)

Table 4. Drug resistant patterns to four anti-tuberculosis drugs

Resistance Pattern	Number of Resistance Isolates (%)
Resistance to any drug	5 (22.7%)
One drug resistance	
INH	1 (4.5%)
RIF	1 (4.5%)
SM	0 (0%)
EMB	1 (4.5%)
Total	3 (13.6%)
Two drug resistance	
INH+SM	1 (4.5%)
INH+RIF	1 (4.5%)
Total	2 (9.0%)
MDR*	1 (4.5%)

EMB: Ethambutal, INH: Isoniazid, RIF: Rifampicin, SM: Streptomycin, *MDR: Multi-drug resistant, resistance to both INH and RIF with or without resistance to other drugs

Drug-susceptibility results were not available for all of the patients. Drug susceptibility test was performed only on 22 *M. tuberculosis* isolates. Out of 22 isolates, 17 (77.2%) were sensitive to all four drugs, whereas five (22.7%) were resistant to one or more of the drugs. The number and rates of resistant patterns to anti-tuberculosis drugs are shown in Table

4. The isolates showed different resistance patterns to four drugs as tested. Single drug resistance rates anti-tuberculosis drugs for isoniazid, rifampicin, ethambutal and streptomycin were 4.5% (n=1), 4.5% (n=1), 4.5% (n=1), 0% (n=0), respectively. Three (13.6%) of isolates were resistant to one drug, two (9.5%) isolates were resistant to two drugs. Resistance to rifampicin was found associated with two drug resistance. At least rifampicin and isoniazid resistant strains multidrug resistance (MDR) was determined in one strain (4.5%).

Among all tuberculosis patients enrolled in this study 39 (69.6%) were completed treatment, 16 (28.5%) were cured and 1 (1.7%) had treatment failure. From the 56 patients evaluated for treatment outcome, 55 (98.1%) had successful treatment outcome. Child with confirmed MDR tuberculosis was completed treatment. No child was reported to have been died and lost to follow up. Patients with only lung involment, smear positive cases, the 15-18 year age group and the new patients had the highest proportion of those cured. Treatment completion was highest among new patients (94.9%). As shown in table 5, there was significant association between treatment outcome and age, site of disease, smear results and culture results ($p<0.05$).

Table 5. Treatment outcome of pediatric pulmonary tuberculosis cases, presented according to do demographic and clinical variables, 2014-2017

Characteristic	Cured Number (%)	Treatment completed Number (%)	Treatment failed Number (%)	Died Number (%)	Lost to follow up Number (%)	*P*-value
Sex						
Female	6 (37,5)	20 (51,3)	0 (0)	0 (0)	0 (0)	0,417
Male	10 (62,5)	19 (48,7)	1 (100)	0 (0)	0 (0)	
Age at diagnosis (years)						
0-5	0 (0)	9 (23,1)	0 (0)	0 (0)	0 (0)	0,007
5-10	0 (0)	4 (10,3)	0 (0)	0 (0)	0 (0)	
10-15	2 (12,5)	14 (35,9)	1 (100)	0 (0)	0 (0)	
15-18	14 (87,5)	12 (30,8)	0 (0)	0 (0)	0 (0)	
Country of birth						
Turkey	13 (81,3)	32 (82,1)	1 (100)	0 (0)	0 (0)	0,893
Other Country	3 (18,8)	7 (17,9)	0 (0)	0 (0)	0 (0)	
Category of patients						
New	14 (87,5)	37 (94,9)	1 (100)	0 (0)	0 (0)	0,617
Relaps	2 (12,5)	1 (2,6)	0 (0)	0 (0)	0 (0)	
Dafaulter	0 (0)	1 (2,6)	0 (0)	0 (0)	0 (0)	
Site of disease						
Pulmonary	16 (100)	32 (82,1)	0 (0)	0 (0)	0 (0)	0,011
Pulmonary+Extrapulmonary	0 (0)	7 (17,9)	1 (100)	0 (0)	0 (0)	
Smear microscopy						
Not performed	0 (0)	13 (33,3)	0 (0)	0 (0)	0 (0)	<0,001
Negative	0 (0)	19 (48,7)	1 (100)	0 (0)	0 (0)	
Positive	16 (100)	7 (17,9)	0 (0)	0 (0)	0 (0)	
Culture						
Not performed	0 (0)	17 (43,6)	0 (0)	0 (0)	0 (0)	0,006
Negative	4 (25)	11 (28,2)	0 (0)	0 (0)	0 (0)	
Positive	12 (75)	11 (28,2)	1 (100)	0 (0)	0 (0)	
Contact history of a tuberculosis patient						
Yes	5 (31,3)	15 (38,5)	0 (0)	0 (0)	0 (0)	0,663
No	11 (68,8)	24 (61,5)	1 (100)	0 (0)	0 (0)	
BCG vaccination status						
Yes	12 (75)	17 (43,6)	0 (0)	0 (0)	0 (0)	0,062
No	4 (25)	22 (56,4)	1 (100)	0 (0)	0 (0)	

DISCUSSION

Tuberculosis is one of the most 10 causes of global death, and the leading cause results from a single infectious agent (above HIV/AIDS). Millions of people have been sufferred from the disease each year. Tuberculosis affects all countries and all age groups, but overall the best estimates for 2017 were that 90% of cases were aged ≥ 15 years and 64% were male[1].

It is difficult to diagnose for children, since most of the signs and symptoms of tuberculosis, one of the most important causes of death in childhood, are not specific to the disease, the sensitivity of diagnostic tests in children is low, and tuberculosis can mimic many diseases. However, the most important factors affecting the disease and mortality rate are the early start of treatment. Therefore, in cases where a laboratory is not possible to prove the disease, clinical and radiological findings should be evaluated together and treatment should be started. The most important step for diagnosis is to suspect the disease. The publication of data on childhood tuberculosis in Turkey is very important in this respect[15].

Children can present with tuberculosis disease at any age but most commonly, in tuberculosis endemic countries, between 1 and 4 years. Pulmonary tuberculosis is the commonest type of tuberculosis in children. Children who develop tuberculosis disease usually do so within 1 year following infection, which is why the presentation of tuberculosis in children is a recent, ongoing indicator of transmission of *M. tuberculosis* among the people[1]. Infants and young children (especially those under 2 years) are at greatest risk of developing severe, disseminated disease associated with a high morbidity and mortality[15]. In the pediatric population, age is one of the risk factors for progression to active disease; cases observed in this study report that the highest infection rates are found in children between 15 and 18 years of age[7]. In a study conducted in Bogota, Colombia, the highest infection rates are found in children under 5 years of age[7].

The presence of a history of contact with the patient with tuberculosis has an important role in the diagnosis of childhood tuberculosis. Tuberculosis infection in children is mostly caused by adults with tuberculosis and the most common form of is household contact[5]. It is difficult for children to produce sputum, and the number of bacilli in sputum is low. Therefore, children are not expected to have index cases. Index for tuberculosis diagnosis is very important in them since tuberculosis is usually transmitted to children from adult infectious tuberculosis patients[6]. Tanir et al. reported to be 118 children with tuberculosis between 2001 and 2003 in Ankara, Turkey. A history of contact with an adult having tuberculosis was observed in 58% of cases[16]. Dilen et al. reported that among 14 cases with pulmonary tuberculosis diagnosed between 2012 and 2014 in Adana, Turkey, the history of in-home contact was found in 50% of the patients and the history of out off-house contact was found in 14.3% of the patients while there was no any history of contact in 35.7% of the patients[5]. In this study, the history of household contact was found in 35.7% of the patients diagnosed with pulmonary tuberculosis while there was no any history of contact in 64.2% of the patients. An index cases could be detected in 13 patients. Two (15.3%) patients had contact history with more than one adult tuberculosis patient.

The symptoms of tuberculosis in pediatric cases are nonspecific, and many researches have been carried out on their clinical and diagnostic significances[9]. The most common clinical findings in tuberculosis are a combination of cough, fever, and night sweats[4]. In a study on 13 infants with pulmonary tuberculosis, fever and night sweats were reported in 21.4% and 35.7% of patients, respectively[17]. Gulec et al. reported that fever (54.9%), cough (51%) and weight loss (29.4%) were the most frequent clinical sign[8]. Turel et al. detected the most common symptoms were long-standing fever (43.1%), cough (69.5%), and night sweats (26.2%)[4]. In our study, the most common symptoms were cough (80.3%), weight loss (73.2%) and night sweating (51.7%).

Although culture becomes the gold standard for diagnosis of tuberculosis in adults, the microbiological diagnosis of tuberculosis by microscopy or culture in children is difficult[18]. Bacteriological confirmation should always be investigate employing using all the existing resources, although is known that pediatric cases are generally paucibacillary[19]. Dilen et al. Found that 28.6% of patients with pulmonary tuberculosis had positive ARB and M. tuberculosis culture growth was observed in 21.4% of patients[5]. In an Indian study only 56.45% of the cases could be microbiologically confirmed[18]. In a previous study, 67.6% of the cases could be confirmed microbiologically[20]. Only 76.7%

of the patients were microbiologically confirmed as having tuberculosis in our study. Microscopy of biological samples were positive for tuberculosis in 53.4%, of cases. *M. tuberculosis* were growth at 61.5% rate in culture. It has been suggested that higher AFB and culture positivity were most likely in patients over 10 years old[9]. Microscopy and culture positivity were high in our study because 76.7% of the patients were older than 10 years old. The researchers reported that these outcomes may be related to restrictions in proper sample collecting in younger children and higher bacillus loads in adolescent patients[9].

In addition to the identification of antimicrobial susceptibility accurate diagnosis and isolation of drug-resistant strains are more important in childhood tuberculosis[8]. Determination of the factor in culture is extremely important especially in terms of antimicrobial resistance. Identification of multiple or single-drug resistance is important in the treatment and determines the drug to be used and its duration[10]. Although multi-drug resistant tuberculosis forms less than 1% of the cases in the United States, a rate has been reported to be as high as 15% from Kazakistan[21]. Gülec et al. reported that isoniazid resistance was found in four cases (7.8%)[8]. There are limited studies on drug resistance in children. Çakır et al. found the rate of resistant tuberculosis in children as high as 48%[23]. Similarly, Kamer et al. detected drug resistance in 42% of culture-positive cases[10]. In recent years, multiple resistance development has been increasing in adult cases, and it is a major problem especially in contacted pediatric patients. Kamer et al. reported drug resistance in 6 cases (7.9%), 2 of whom developed multiple-drug[10]. In the present study, drug sensitivity tests was performed for the *M. tuberculosis* complex strains isolated from 22 cases. Out of 22 cases, 17 (77.2%) were sensitive to all four drugs, whereas five (22.7%) were resistant to one or more of the drugs. MDR tuberculosis (isoniazid + rifampicin resistance) was detected in one patient. Drug resistance was found in 5 (8.9%) cases in all patients in our study. According to the data of our country, the resistance status in pediatric patients varies between 2.2% and 7.9%. The rate of resistant cases was found smilarly to other studies in our country. Determination of multiple or single drug resistance is important in the treatment and determines the duration of the drug to be used[10]. Given this relatively high drug resistance rate, we suggest recommend that drug susceptibility testing should be performed. On the other hand, any delay in identifying drug-resistant tuberculosis may rise childhood mortality and morbidity[8].

Children treated for tuberculosis possess good treatment results in spite of comorbidities. That children could have much better treatment results than adults raises the possibility that children may be specifically fitted to do well with shorter, less intense treatment regimens[13]. In a study conducted in Accra, a treatment result was documented for 214 children (97.7%). Of these, 90.7%, were successfully treated consisting of 81.3% who completed treatment and 9.4% who were cured[2]. Gulec et al. reported that all patients responded well to the treatment except one patient with nephrotic syndrome and miliary tuberculosis died during follow-up[8]. Studies such as Yunda et al. evaluated the pulmonary tuberculosis in pediatric patients in Colombia, patients who received treatment were classified as treated in 14 (22.9%) cases and treatment in 22 (36.1%) cases; failure was reported in 1 (1.6%) case. Results for no institutional follow-up are unknown in 19 cases (31.2%)[7]. In our study, traetment outcome was detected for all patients (100%). Fifty-five of these, 98.1%, were successfully treated consisting of 69.6% who completed treatment and 28.5% who were cured. One (1.7%) patient had treatment failure. The case classified as treatment failure was a miliary tuberculosis. The drug susceptibility testing was performed without documented resistance. No child was reported to have been died. The treatment success recorded in our study may reflects good case management.

The main limitation of our study is that it is a retrospective, single-region study with a limited number of pediatric patients aged ≤18 years. The studies of epidemiological and clinical characteristics of pediatric pulmoner tuberculosis on the large series of cases may be essential for early diagnosis and treatment. Multicenter studies are required to provide more illustrative data in Turkey.

In conclusion, this study highlights the epidemiologic features and treatment outcomes of children with pulmonary tuberculosis in Adana, Turkey. Pediatric tuberculosis is a marker of the fact that tuberculosis in adults is not controlled and is the basis of adult tuberculosis patients. Therefore, the identification and effective treatment of pediatric tuberculosis in the community is an important point in the fight against tuberculosis. Although tuberculosis is common in children, there is little research that investigates the issues related to this field. Indeed,

children are often excluded from research. Results of this study helps to achieve a better diagnostic approach in this population.

Yazar Katkıları: Çalışma konsepti/Tasarımı: PE, ATA; Veri toplama: PE, ATA; Veri analizi ve yorumlama: PE, ATA; Yazı taslağı: PE; İçeriğin eleştirel incelenmesi: PE, ATA; Son onay ve sorumluluk: PE, ATA; Teknik ve malzeme desteği: ATA; Süpervizyon: PE; Fon sağlama (mevcut ise): yok.
Etik Onay: Bu çalışma için Çukurova Üniversitesi Tıp Fakültesi Girişimsel Olmayan Klinik Araştırmalar Etik Kurulundan 02.11.2018 tarih ve 82/36 sayılı kararı ile etik onay alınmıştır.
Hakem Değerlendirmesi: Dış bağımsız.
Çıkar Çatışması: Yazarlar çıkar çatışması beyan etmemişlerdir.
Finansal Destek: Yazarlar finansal destek beyan etmemişlerdir.
Author Contributions: Concept/Design : PE, ATA; Data acquisition: PE, ATA; Data analysis and interpretation: PE, ATA; Drafting manuscript: PE; Critical revision of manuscript: PE, ATA; Final approval and accountability: PE, ATA; Technical or material support: ATA; Supervision: PE; Securing funding (if available): n/a.
Ethical Approval: For this study, ethics approval was obtained from Çukurova University Faculty of Medicine non-interventional clinical research ethics committee with Decision No. 82/36 dated 02.11.2018.
Peer-review: Externally peer-reviewed.
Conflict of Interest: Authors declared no conflict of interest.
Financial Disclosure: Authors declared no financial support

REFERENCES

1. World Health Organization. Global Tuberculosis Report 2018. http://www.who.int/tb/publications/global_report/en/ (date of access 2020 May 01).
2. Ohene SA, Fordah S, Boni PD. Childhood tuberculosis and treatment outcomes in Accra: a retrospective analysis. BMC Infect Dis. 2019;19:6-9.
3. Keshtkar Jahromi M, Sharifi-Mood B. Pulmonary tuberculosis in children. Int J Infect. 2014;1(3):e21116. http://intjinfection.com/articles/14737.html.
4. Turel O, Kazanci S, Gonen I, Aydogmus C, Karaoglan E, Siraneci R. Paediatric tuberculosis at a referral hospital in Istanbul: Analysis of 250 cases. Biomed Res Int. 2016;2016:1-6.
5. Dilen MF, Çelik T, Tolunay O, Çelik U. Clinical features in childhood tuberculosis followed in our clinic. J Pediatr Inf. 2018;12(4):e129-e34.
6. Gencer H, Dalgıç N, Kafadar I, Kabakçı D, Öncül U. Retrospective evaluation of 35 pediatric tuberculosis cases proven by histopathological and/or microbiological analysis. J Pediatr Inf. 2015;9:97-101.
7. Yunda LF, Sepúlveda EV, Herrera KC, Moreno C. Pulmonary tuberculosis in a pediatric reference hospital in Bogota, Colombia. Int J Mycobacteriol. 2017;6:258-63.
8. Gulec SG, Telhan L, Koçkaya T, Erdem E, Bayraktar B, Palanduz A. Description of pediatric tuberculosis evaluated in a referral center in Istanbul Turkey. Yonsei Med J. 2012;53:1176-82.
9. Bayhan GI, Tanır G, Metin O, Şimsek H, Aydın-Teke T, Öz FN et al. Pediatric tuberculosis in Turkey: a review of 8-years period in a tertiary care hospital. Turk J Pediatr. 2015;57:431-38.
10. Kamer I, Sütçü M, Acar M, Erol OB, Hançerli Törün S, Salman N et al. Pediyatrik tüberküloz: Bir üniversite hastanesinin beş yıllık deneyimi. J Child. 2017;17:43-9.
11. Ian Kitai MB BCh, Shaun K Morris MD MPH, Faisal Kordy MD, Ray Lam MN-ANP PHCNP. Diagnosis and management of pediatric tuberculosis in Canada. CMAJ. 2017; 9,189: E11-6. doi: 10.1503/cmaj.151212.
12. Babalık A, Kılıçaslan Z, Kızıltaş Ş, Gencer S, Öngen G. Aretrospektif case-control study, factors affecting treatment outcomes for pulmonary tuberculosis in Istanbul, Turkey. Balkan Med J. 2013;30:204-10.
13. Harausz EP, Garcia-Prats AJ, Law S, Schaaf HS, Kredo T, Seddon JA et al. Treatment and outcomes in children with multidrug-resistant tuberculosis: A systematic review and individual patient data meta-analysis. PLoS Med. 2018;15(7):e1002591.
14. Biruk M, Yimam B, Abrha H, Biruk S, Amdie FZ. Treatment outcomes of tuberculosis and associated factors in an Ethiopian university hospital. Adv Public Health. 2016;2016:1-9.
15. Guidance for national tuberculosis programmes on the management of tuberculosis in children. World Health Organization. 2nd Ed. ISBN 978 92 4 154874 8. https://www.who.int/tb/publications/childtb_guidelines/en/(date of access: 2020 May 19).
16. Tanır G, Akın A, Aydemir C, Üner Ç, Ceyhan İ. The diagnosis of definitive or probable tuberculosis and latent tuberculosis infection in children with suspected tuberculosis. Tuberk Toraks. 2005;53:259-64.
17. Bayhan Gİ, Ekşioğlu AS, Kitiş Çelik B, Tanır G. Pulmonary tuberculosis in infants less than one year old: Implications for early diagnosis. Tuberk and Toraks. 2011;59:36-42.
18. Gupta N, Kashyap B, Dewan P, Hyanki P, Singh NP. Clinical spectrum of pediatric tuberculosis: A microbiological correlation from a tertiary care center. J Trop Pediatr. 2019;65:130-38.
19. Berti E, Galli L, Venturini E, Martini De M, Chiappini E. Tuberculosis in childhood: a systematic review of national and international guidelines. BMC Infect Dis. 2014;14:S3.
20. Cano APG, Romaneli MTN, Pereira RM, Tresoldi AT. Tuberculosis in pediatric patients: How has the diagnosis been made? Rev Paul Pediatr. 2017;35:165-70.
21. Cruz AT, Starke JR. Pediatric tuberculosis. Pediatr Rev. 2010;31:13-25.