Pediatric pulmonology in a developing country: our focus

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This study was designed to determine the profile of our pediatric pulmonology unit in Turkey, a developing country, by investigating the patients admitted to our unit for the first time.

Our objectives were: to determine the profile of patients admitted for the first time, to compare their initial diagnoses before referral to our hospital with the diagnoses determined in our unit, to determine the definitive diagnoses for patients requiring advanced intervention with invasive diagnostic methods, and to follow the treatments, operations and invasive-noninvasive mechanical ventilation practices.

With these objectives in mind, the records of 412 patients who visited the pediatric pulmonology clinic within a six-month period were reviewed. The referral diagnoses, consisting mostly of primary ciliary dyskinesia, recurrent lung infections caused by immune deficiency and bronchiectasis, as well as definitive diagnoses were recorded. Tuberculosis (14%), cystic fibrosis (7.8%), bronchiectasis (4.6%), immune deficiency (1.6%), hydatid cyst (2%), and primary ciliary dyskinesia (1%) were the most commonly diagnosed diseases.

Final diagnosis in 145 of the 412 patients (35.2%) differed from the referral diagnosis.

Consanguineous marriages are encountered more commonly in developing countries like Turkey, leading to an increased incidence of genetic diseases such as primary ciliary dysgenesis, cystic fibrosis and immune deficiencies. Infectious diseases such as hydatid cyst and tuberculosis are also common.

In any country in which there is a unique distribution of diseases, in other words, a characteristic and unique disease spectrum, courses and instructional fellowship programs should be arranged accordingly.

Key words: pediatric pulmonology, child, pediatric respiratory tract diseases.

The acceptance in Turkey of pediatric pulmonology as a separate division and a super-specialty discipline under the purview of general pediatrics has been a long and challenging process. While pediatric pulmonology initially focused primarily on tuberculosis (TB), asthma and cystic fibrosis (CF), subjects like bronchopulmonary dysplasia, sudden infant death syndrome, bronchiolitis, cor pulmonale, acute and chronic respiratory tract diseases, gastroesophageal reflux (GER), and exposure to cigarette smoke emerged later as areas of increasing interest. Crucial diagnoses and findings do not escape notice in pediatric pulmonology centers when they are sub-specialized, and the patient diagnosis is not delayed.

Subsequently, other problems such as pulmonary involvement in systemic diseases and effects of chemotherapeutic drugs on the lungs have widened the spectrum of pediatric pulmonology[1,2]. Our aim in this report was to determine the profile of the pediatric pulmonology unit by investigating the patients admitted to our unit for the first time.

Our objectives were:

• To determine the profile of patients admitted for the first time within a six-month period.

• To compare the initial diagnoses of the patients before their referral to our hospital with the diagnoses determined in our unit.

• To determine the final diagnoses for the patients requiring advanced intervention with invasive diagnostic methods.

• To follow the treatments, operations and invasive-noninvasive mechanical ventilation practices applied in patients who received special diagnoses.

Material and Methods

Patients who were admitted to the Hacettepe University Faculty of Medicine Pediatric Pulmonology Unit in Ankara for the first time between 1 June 2005 and 31 December 2005 were enrolled in the study. Our unit is a tertiary health care service for pediatric pulmonology in Turkey.

Patients included in the study were referred to our clinic directly by a primary care physician, local general hospitals or other university hospitals.

Results

Four hundred and twelve patients (172 F [41.8%], 240 M [58.2%]) were admitted to our department for the first time within the six–month period of 1 June – 31 December 2005. One hundred and ninety-nine (48.3%) of the 412 patients admitted for the first time were from Ankara, whereas 213 (51.7%) were from different rural areas of Turkey.

The referring centers and numbers of the patients are shown in Table I.

A comparison of the initial and final diagnoses of the patients revealed some differences (Table II). Final diagnoses in 145 of the 412 patients (35.2%) differed from their referral diagnoses. Diagnoses of the patients are shown in Table III. Two of the 30 patients (6.6%) admitted with an initial diagnosis of CF were concluded to have recurrent lung infection. A total of 32 patients (7.9%) were diagnosed as CF: 1 had been referred to our hospital for anemia and constipation, and 2 had been referred for a family history of CF in siblings and an aunt. Eleven of the patients were hospitalized for treatment. All patients' families were educated regarding CF. All these patients were evaluated with a multidisciplinary approach. The sweat test was applied to 1378 patients during the six-month period in our unit.

Nine patients (2%) received a diagnosis of hydatid cyst and were administered albendazole. Six patients were treated with percutaneous drainage and 3 patients were operated.

Seven patients (1.7%) referred for chronic cough with diagnoses of foreign body aspiration (FBA) and recurrent lung infection were diagnosed as immune deficiency.

Bronchiolitis obliterans was diagnosed in 6 patients (1.5%): 3 of these patients were referred to us with recurrent lung infection while the other 3 had an initial diagnosis of bronchiolitis obliterans. Three patients were diagnosed as bronchopulmonary dysplasia. Four patients (1%) received a diagnosis of congenital lobar emphysema and underwent lobectomy. Of the patients with chronic respiratory failure, 4 (1%) were given home ventilators and 4 (1%) were given bilevel positive airway pressure (BIPAP) devices. Of 103 patients investigated for chronic cough and recurrent lung infection, 42 received a diagnosis of GER. Two patients had intestinal malrotation and 1 patient had pharyngeal dyskinesia. Atelectasis was detected in 15 patients (3.6%) (Table I).

Flexible bronchoscopy was performed in 47 (11%) patients for diagnosis and treatment. Four patients received a diagnosis of cytomegalovirus (CMV) pneumonia with bronchoalveolar lavage fluid examination. Open lung biopsy was performed in 2 patients for diagnostic evaluation. One of the patients was diagnosed as chronic infantile pneumonia. Seven patients were referred to us before tumor necrosis factor (TNF)-α treatment from other clinics of our hospital. Four patients who had acute lymphocytic leukemia in remission were followed-up for pulmonary function after chemotherapy. Five patients were referred to us for spinal muscular atrophy, 7 patients for congenital muscular dystrophy, 1 patient for congenital neuropathy, 3 patients for pectus excavatum, and 2 patients for scoliosis. Two of these patients were followed with a home ventilator, 2 with BIPAP and 1 underwent a gastrostomy. Eight patients were admitted

Table I. Referral Center of the Patients

Referral center	Number of patients (n: 412)
Family demand	27 (6.5%)
General hospital	36 (8.7%)
Other university hospitals	68 (16.5%)
Our university hospital	
Pediatric clinic	105 (25.5%)
Pediatric emergency clinic	48 (11.7%)
Other clinics	128 (31.1%)

with mental-motor retardation and recurrent lung infection; 1 of them was operated with a diagnosis of intestinal malrotation.

Discussion

The process of establishing and approving pediatric pulmonology as a separate branch under the purview of pediatrics has been long and arduous. Initially, adult pulmonary disease specialists dealt with pediatric pulmonology. Over time, educational programs were developed and led to the emergence of pediatric pulmonologists. Adult pulmonary disease specialists Bates, Riley, Permutt, Fishman, and Chernick were involved in this process. Pediatric pulmonologists Clement Smith and John Clements pioneered the development of pediatric pulmonology throughout the 1950s and early 60s. In 1950, the Pediatric Pulmonology Division of the American Academy of Pediatrics was established. Scholarship applications from the Cystic Fibrosis Foundation, which began in 1965, and the acceptance and support of the American National Health Institution's Pulmonology Division for Pediatric Pulmonology as a separate province led to the further development of this division and an increase in the related studies. The main activity of the European Specialists in Pediatrics during 2001 focused on completing the list of pediatric pulmonology units in Europe. To comprise this list, the Pediatric Assembly of the European Respiratory Society and Committee on Pediatric Respiratory Training in Europe were assembled. Related information was collected by local delegates including volunteers from members of the European Union and from some countries outside the European Union, and the list was completed in 2000[1-4]. Turkey was one of the countries outside the European Union that participated on a voluntary basis.

Pediatric pulmonology is a newly developing subspecialty of pediatrics in Turkey, and the journey for its inclusion in general pediatrics as a separate division was prolonged and challenging. In our country, since pediatric allergy and asthma units are relatively common and focus primarily on asthma and allergic disease, there was a need for pediatric pulmonology units to deal mainly with the other pulmonary diseases.

In the first years, pediatric pulmonology in Turkey was concerned mainly with TB, empyema, bronchiectasis, acute and chronic respiratory tract infections, the relationship between respiratory and gastrointestinal system functions (especially GER), and subjects like exposure to cigarette smoke. In recent years, the patient spectrum of pediatric pulmonology has expanded due to lung involvement in systemic diseases, the effects of chemotherapeutic drugs on the lungs, and usage of TNF-α blockers in inflammatory diseases, which increase susceptibility to TB. Usage of invasive methods for diagnosis occurred in recent years.

One hundred and ninety-nine (48.3%) of our patients were admitted from Ankara, whereas 213 (51.7%) were admitted from different rural areas. This is because pediatric pulmonology specialists are only available in certain cities/institutions. The referral of 121 patients (30.2%) from universities and general hospitals can be attributed to the same reason. While CF and congenital anomalies are more common in developed countries, in developing countries like Turkey where consanguineous marriages are seen at high rates, primary ciliary dyskinesia (PCD) and immune deficiency are observed frequently in addition to CF. Thus, in countries like Turkey in which the rate of consanguineous marriages is high, these diseases must be considered. The mutation carrier frequency in Turkish CF patients was found as 1 in 50[5].

Table II. Initial and Final Diagnoses of the Patients

Initial diagnosis	Number of patients N: 267	Different diagnosis N: 145	Different final diagnoses
Recurrent lung infection	46	46 (100%)	Adenovirus (2) GER (8) PCD (3) Atelectasis (6) Immune deficiency (3) Bronchiolitis obliterans (6) Bronchiectasis (8) CMV pneumonia (1) Intestinal malrotation (2) Swallowing dysfunction (1) Asthma (6)
Chronic cough	57	53 (96%)	Atelectasis (5) Adenoid vegetation (2) Bronchopulmonary dysplasia (2) GER (25) FBA (1) Laryngomalacia (4) Bronchiectasis (10) Immune deficiency (3) CF (1)
CF	30	2 (6.6%)	Recurrent lung infection (2)
Lung infection	19	9 (47.3%)	Atelectasis (4) GER (3) Asthma (1) Upper respiratory tract infection (1)
TB disease	9	4 (44.4%)	TB infection (2) Bronchiectasis (2)
TB infection	54	7 (12.9%)	Normal (1) TB disease (1) GER (3) Bronchiectasis (2)
Bronchiolitis obliterans	7	3 (42.8%)	CMV pneumonia (1) Viral pneumonia (1) Chronic infantile pneumonia (1)
Bronchiectasis	13	2 (15.3%)	PCD (1) GER (1)
Atelectasis	3	1 (33.3%)	Congenital lobar emphysema (1)
Angioneurotic edema	1	1 (100%)	Yellow nail syndrome (1)
Loeffler pneumonia	1	1 (100%)	Pulmonary hemosiderosis (1)
Pulmonary hemosiderosis	3	1 (33.3%)	Bronchiolitis obliterans (1)
Hemoptysis	2	2 (100%)	Hematemesis (1) Psychosomatic disease (1)
Anemia	1	1 (100%)	CF (1)
Tracheoesophageal fistula	1	1 (100%)	GER (1)
FBA	8	4 (50%)	Congenital lobar emphysema (2) IgA deficiency (1) CMV pneumonia (1)
Wheezy infant	8	3 (37.5%)	CMV pneumonia (1) Adenovirus pneumonia (1) GER (1)
Sarcoidosis	1	1 (100%)	Interstitial pneumonia (1)
Dyspnea	1	1 (100%)	Subglottic stenosis (1)
CMV pneumonia	1	1 (100%)	Laryngomalacia (1)
Meningitis and pulmonary infection	1	1 (100%)	TB disease (1)

CF: Cystic fibrosis. CMV: Cytomegalovirus. FBA: Foreign body aspiration. GER: Gastroesophageal reflux, PCD: Primary ciliary dyskinesia. TB: Tuberculosis.

It is estimated that nearly 4 million children die each year from acute respiratory illness, most of them in developing countries. Poverty, with its accompanying nutritional deficiency, particularly of vitamin A and zinc, plays a major role in the prevalence and mortality from acute respiratory illnesses in children[6]. It is estimated that 250 million people worldwide have asthma, which is now the most prevalent chronic disease in childhood[7]. There are 8 million new cases of active TB annually, with the worst annual increase in TB in Africa because of human immunodeficiency virus (HIV) infection. Because of this global epidemic of respiratory disease burden, a Forum of International Respiratory Societies has recently been formed[8]. Pediatric pulmonologists will need to play a prominent role in this international effort in the future.

Tuberculosis (TB) is an important public health problem with high mortality and morbidity rates throughout the world. There are differences between the developed and the developing countries in the incidence of the disease. The TB incidence in Turkey was 28/100,000, and its prevalence was 45/100[9,10]. The proportion of childhood TB cases to all cases is 9% in Turkey. According to the 2005 disease load (burden) data of the Ministry of Health, TB takes eighth place in disease load (burden) and death ranking for children under the age of 15[11,12]. Diagnosis of childhood TB is more difficult than of adult TB.

It is difficult for children to expectorate sputum, and the number of bacilli in the sputum is lower. Therefore, children with TB are not supposed to be index cases. It is important to detect index cases and to prevent transmission to others. Following up the therapies of these patients and determining the resistance of the bacilli to anti-TB drugs are also important. For these reasons, these patients suffering from childhood TB must be monitored by pediatric pulmonologists. The patients we diagnosed as TB infection were referred to our department from other hospitals. We suggest that pediatric pulmonologists are needed for treatment and follow-up of these patients at present. One of the other most common reasons for admission to the pediatric pulmonology clinic was chronic cough and recurrent lung infection. For the patients who were referred to our unit with initial diagnoses of chronic cough and recurrent lung infection, 96-100% of these diagnoses

Table III. Final Diagnoses of the Patients Admitted to our Unit

Number of patients N: 233	Final diagnosis
51	Tuberculosis infection
7	Tuberculosis disease
42	Gastroesophageal reflux
32	Cystic fibrosis
19	Bronchiectasis
15	Atelectasis
10	Laryngomalacia
9	Hydatid cyst
7	Immune deficiency
6	Bronchiolitis obliterans
3	Bronchopulmonary dysplasia
2	Wegener granulomatosis
3	Pulmonary hemosiderosis
4	Congenital lobar emphysema
4	Foreign body aspiration
7	Bronchomalacia
4	Cytomegalovirus pneumonia
2	Adenovirus pneumonia
1	Yellow nail syndrome
1	Habitual cough
4	Primary ciliary dyskinesia

were changed after evaluation in our unit. This illustrates the significance of evaluation by a pediatric pulmonologist for patients with these diagnoses. It is seen in Table II that chronic cough is of concern for the community and pulmonologists in terms of economy and as well as time consumption, and invasive procedures are needed to determine the cause of the chronic cough.

The last report regarding the disease burden in our country shows that lower airway diseases ranks second for the preventable deaths before the age of 15. Thus, many diseases like TB, CF, pneumonia, interstitial lung diseases, sarcoidosis, and congenital respiratory malformations can be seen in childhood. For the diagnosis and therapy of these complex diseases, many diagnostic procedures like plethysmography and invasive endoscopic procedures like bronchoscopy should be performed. For these reasons, pediatric pulmonology, which requires special education and experience, must be a high specialization area in our country, as in the whole world.

Post-infectious bronchiectasis is not a rare entity in our country, although bronchiectasis usually results from CF in western countries. As consanguineous marriage is common in Turkey, PCD and immune deficiencies should be investigated in such patients. In our study group, we diagnosed CF and PCD as immune deficiency.

Highly atopic children were treated by pediatric allergists, but children with asthma by and large continued to be treated by family practitioners and pediatricians rather than allergists or pulmonologists. In our country, general practitioners and family practitioners have theoretical and practical poverty in asthma diagnosis and therapy; thus, all wheezy children are being followed as asthma and many diseases such as CF, PCD and congenital airway malformations can be diagnosed late. For these reasons, before making the asthma diagnosis, these patients must be evaluated by a pediatric pulmonologist. The patients with chronic cough who were consulted to us received varied final diagnoses.

Thirty-two patients with CF received a multidisciplinary education, and education was also provided to their families, as in European countries and America. Multidisciplinary education is important in CF disease. As declared in the last European consensus report, the Pediatric Pulmonology Division must cooperate and follow-up patients in cooperation with Pediatric Gastroenterology, Pediatric Endocrinology, Pediatric Surgery, Nutrition and Dietetics, and Physical Therapy and Rehabilitation divisions[13].

Pediatric pulmonology has the greatest importance for the diagnosis and follow-up of CF patients. Early diagnosis and appropriate therapies help CF patients to reach adulthood and facilitate a decent quality of life[13].

In developing countries, hydatid cyst is also an important public health problem. Patients with liver and lung hydatid cyst can admit with symptoms like chest pain, abdominal pain, expectoration of clear fluid, hemoptysis, and cough. All our patients were referred from general hospitals after determining this diagnosis. After initiation of albendazole treatment, liver cyst drainage was performed in six of them, and three of them were operated. In the course of decision-making, each patient was evaluated separately by each of the three divisions, and a decision regarding the treatment process was made. In their follow-up, albendazole treatment was planned and stopped according to evaluation of liver hydatid cysts with ultrasonography and lung hydatid cysts with X-ray and, if needed, tomography[14].

Bronchoscopy is an important diagnosis and treatment method in pediatric pulmonology departments[15]. Fiberoptic bronchoscopy (FOB) is one of the major tools for evaluating respiratory disorders in children, and its diagnostic value is widely accepted[16]. It can be useful therapeutically as well[17]. The first task of the bronchoscopist is the visualization of upper and lower airways, including both their morphology and mobility. The associated procedures, such as bronchoalveolar lavage (BAL), bronchial brushing and endobronchial biopsies, permit samples to be taken to gain more information about inflammatory processes involved in different airway diseases.

All these procedures carried out during FOB, if performed by skilled physicians working with a good team, have been proven to be safe and useful, without significant side

effects[17]. In patients with persistent stridor, FOB can help to diagnose different forms of laryngomalacia or aspiration syndromes. Tumors are rarely detected as the cause of stridor[18]. Direct visualization of the lower airways is helpful in diagnosing bronchial stenosis. The cause of bronchial stenosis can be intrabronchial (e.g. foreign bodies[18], granulation tissue, mucus plugs, tumors such as bronchial carcinoids and leiomyomas[19,20]) or extrabronchial (lymphadenopathy and mediastinal tumors). The prevalence of different causes varies between centres[21]. BAL allows the study of cells and mediators coming from the bronchoalveolar compartment and the detection of bacteria, viruses, fungi, and protozoa. In asthmatic patients, it allows the study of inflammatory processes in the lower airways. In these patients, BAL cell count does not necessarily reflect that of bronchial mucosal biopsies[22,23], and combining BAL and biopsy can give more information about inflammatory mediators than either technique alone[24]. BAL cell count and culture is also occasionally useful in making a definitive diagnosis of diffuse lung disease in children[25]. BAL can be used therapeutically. Its role in the treatment of alveolar proteinosis and the removal of inhaled material from lower airways is well known. Another example is the clearance of inhaled mineral oil, used as a purgative agent for partial bowel obstruction due to Ascaris lumbricoides[26], or of inhaled skin oils, used for baby care. Bronchoscopy, BAL and biopsy led us in the diagnosis and follow-up of the patients.

Neuromuscular diseases cause chronic respiratory insufficiency and carbon dioxide retention; these patients must be followed regularly for invasive and noninvasive mechanical ventilation needs. Two of 13 patients who were followed received mechanical ventilator support and two other patients received invasive ventilator support; they were included in the follow-up and their families were educated regarding the use and care of the instruments, as well as regarding aspiration[27,28].

When evaluating the patients' initial referral diagnoses, it could be seen that those referred for recurrent lung infection were diagnosed differently, as intestinal malrotation, swallow dysfunction, bronchiolitis obliterans, and habitual cough. While some of the patients referred to us for TB were confirmed as TB, others were determined as bronchiectasis and "other" diagnoses. In one patient referred with an initial diagnosis of atelectasis, congenital lobar emphysema was detected, and another patient referred for bronchoscopy with a diagnosis of FBA was later diagnosed as immune deficiency. In patients referred to us with an initial diagnosis of hemoptysis, hematemesis and psychosomatic illness diagnoses were determined, while another patient referred for angioneurotic edema was diagnosed as yellow nail syndrome.

If we consider especially the importance of early diagnosis for such diseases as TB and pneumonia and diseases that can be diagnosed in childhood but persist into adulthood, we have no doubt that, in the near future, pediatric pulmonology will be an important high specialization area in our country, as in the United States and European nations.

In conclusion, pediatric pulmonology is a newly developing branch of pediatrics in our country. Patients with diseases like CF, bronchiolitis obliterans, bronchiectasis, hydatid cyst, and pulmonary hemosiderosis must be assessed and treated, and their families must be educated by a pediatric pulmonologist, who is more knowledgeable and experienced in these diseases. When the differences between initial and final diagnoses and the indications of invasive diagnostic methods are taken into consideration, the necessity of pediatric pulmonologists is obvious.

We suggest that in any country in which there is a unique distribution of diseases, in other words, a unique characteristic disease spectrum, courses and instructional fellowship programs should be designed accordingly.

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