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THE ROLE OF VIRUSES AND MYCOPLASMA PNEUMONIAE IN LOWER RESPIRATORY TRACT INFECTIONS IN CHILDHOOD*

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Acute lower respiratory tract infections are one of the major causes of childhood morbidity and mortality in developing countries. This study was undertaken at Hacettepe University Children's Hospital to determine the role of viruses and *Mycoplasma pneumoniae* in respiratory tract infections in children. Eighty-three patients with lower respiratory tract infections were selected at random from among the children admitted to the hospital for evaluation of respiratory symptoms. Acute and convalescent serum samples were collected from all patients for the complement-fixation test and the following antigens were used: respiratory syncytial virus (RSV), adenovirus, parainfluenza virus Type 1, influenza viruses A and B, and *Mycoplasma pneumoniae*. The test was positive in 39 of 83 patients (47 %), and RSV was the most frequent agent detected serologically (15.7 %). *Key words: lower respiratory tract infection, respiratory syncytial virus, viral respiratory infection, Mycoplasma pneumoniae.*

Acute lower respiratory tract infections are an important cause of pediatric morbidity and mortality throughout the developing world[1]. There are about 4 million children in the world under the age of five who die each year from acute respiratory infections. This figure constitutes 27 percent of all childhood deaths in this age group[1].

Although bacteria can cause significant diseases of the respiratory tract, it has been possible to establish them as causative agents in only a small proportion of such illnesses. Respiratory syncytial virus (RSV), adenovirus, parainfluenza virus, influenza viruses and *Mycoplasma pneumoniae* are the most important pathogens causing lower respiratory tract infections in childhood[2].

The present study was undertaken at Hacettepe University Children's Hospital to determine the role of viruses and *Mycoplasma pneumoniae* in lower respiratory tract infections in children in Turkey.

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Material and Methods

The study population consisted of 77 out-patients and six hospitalized patients with lower respiratory tract infections who had been selected at random between November 1988 and January 1989 for inclusion in this study.

The illnesses were considered acute if the symptoms of the respiratory disease had been present for less than one month. Only patients with acute illnesses were included in the study.

Lower respiratory tract diseases were defined as infections of the epiglottis, larynx, trachea, and the lungs[2]. These diseases were characterized as croup, tracheobronchitis, bronchiolitis, or pneumonia. Croup was diagnosed by a hoarse barky cough and inspiratory stridor with or without drooling; tracheobronchitis by a cough and rhonchi; bronchiolitis by inspiratory and/or expiratory wheezing without radiographic evidence of consolidation, and pneumonia by rales and radiologic evidence of consolidation or patchy infiltrates[2].

At the first presentation, a history of symptoms related to lower respiratory tract disease, such as cough, fever, tachypnea, wheezing, dyspnea, and cyanosis, was noted. All patients were systematically examined by the same doctor.

The following tests were performed on each patient enrolled in the study: complete blood count, throat culture, chest X-ray and complement-fixation test of sera for serological detection of the agents involved.

Acute and convalescent sera samples were obtained from all patients and were used for complement-fixation tests performed at intervals of 12 and 21 days[3].

Paired sera from 83 patients were studied by means of a microtechnique in which two units of antigens and complement were used simultaneously. RSV, adenovirus, parainfluenza virus Type 1, influenza viruses A and B, and *Mycoplasma pneumoniae* antigens were used. The test was considered positive if there was at least a four-fold rise in antibody titers between the first and second serum specimens.

Results

There were 25 females and 58 males. The mean age was 33 months. Thirty percent of the patients were under one year and 68.5 percent under three years of age. There was a 2.7: 1 male predominance in all groups (Fig. 1).

Cough was the most frequent symptom while cyanosis was the least encountered symptom. Table I lists the physical findings of all patients.

The age-specific frequencies of the clinical pictures are shown in Table II. The positive results of the complement-fixation tests according to age group are

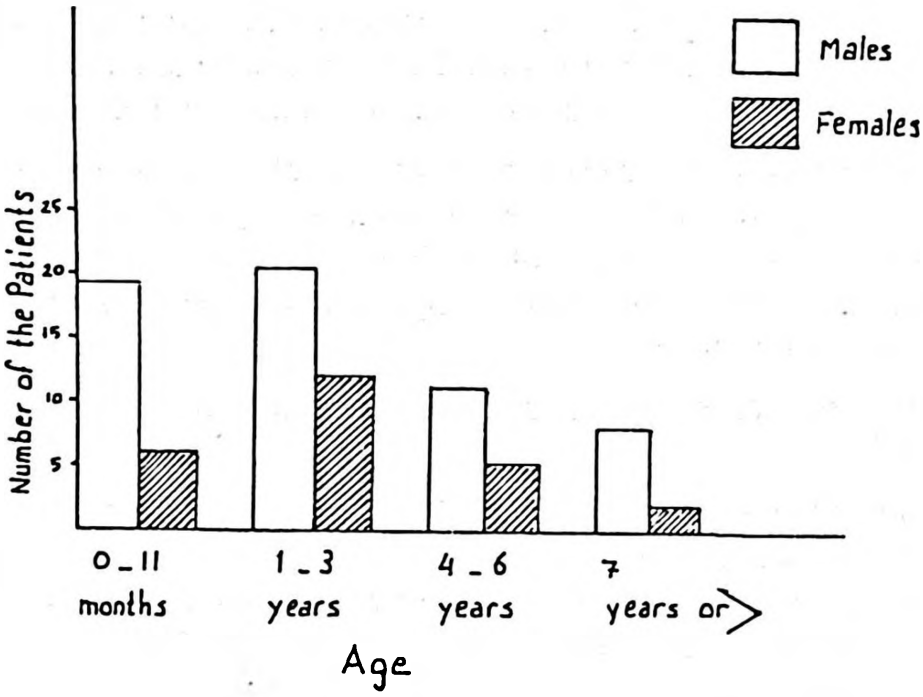

Fig. 1: Age and sex distribution of patients.

TABLE I: Clinical Findings of Patients

Clinical Findings	No. of Patients
Rales	73 (87 %)
Fever	59 (71 %)
Tachycardia	30 (36 %)
Rhonchi	29 (34 %)
Wheezing	20 (24 %)
Tachypnea	16 (19 %)
Cyanosis	4 (4.8 %)

TABLE II: Clinical Picture Distribution According to Age Group

Clinical Diagnosis	0-11 Mos	1-3 Years	4-6 Years	≥ 7 Years	Total
Pneumonia	7	19	12	9	47 (56.6 %)
Bronchiolitis	15	11	2	1	29 (35 %)
Croup	3	1			4 (4.8 %)
Tracheobronchitis		1	2		3 (3.6 %)
Total	25	32	16	10	83 (100 %)

shown in Table III. Thirty-nine of the 83 paired sera were positive and two had serological evidence of infection with more than one agent.

Seriologically, RSV was found to be the agent most frequently associated with lower respiratory tract infections followed by adenovirus, parainfluenza virus Type 1, *Mycoplasma pneumoniae,* and influenza viruses A and B (Table III).

The results in relation to the clinical presentation of the diseases are shown in Table IV. The complement-fixation test results were positive in 42 percent of pneumoniae patients, 58 percent of bronchiolitis patients and 66 percent of tracheobronchitis patients. No etiological agent was detected serologically in the sera of the patients with croup.

Group A *beta-hemolytic streptococcus* was isolated from the throat cultures of seven patients.

A white blood cell count of more than 10,000/mm^3 was noted in 18 of the 39 patients with positive complement-fixation tests. The differential count noted lymphocyte predominance in 20 of these 39 patients, however, polymorphonuclear leukocytes were predominant in all four of the patients infected with *Mycoplasma pneumoniae.*

TABLE III: Agents Serologically Detected in Relation to Age

Agent	0-11 Mos	1-3 Years	4-6 Years	≥ 7 Years	Total (%)
RSV	6	3	3	1	13-15.6
Adenovirus	1	5	1	2	9-10.8
Parainfluenza 1	3	3		2	8-9.6
M.pneumoniae		2	2		4-4.8
Influenza A		1		1	2-2.4
Influenza B	1				1-1.2
Influenza A plus		1			1-1.2
Parainfluenza 1 Influenza A plus				1	1-1.2
RSV					
Total	11	15	6	7	39-47

Most of the symptoms and signs of the patients resolved in a short period of time. A patient with an adenovirus infection was later diagnosed as having asthma. Another patient with influenza A and parainfluenza Type 1 virus infections concomitantly showed no improvement and died in three months.

TABLE IV: Agents in Relation to Clinical Condition

Diagnosis	No. of Patients tested	Number of Patients with Serological Evidence of Infection: RSV	Para 1	Adeno V.	MP	Inf A	Inf B	Inf A + Para 1	Inf A + RSV	Total
Pneumonia	47	6	4	4	3	1	–	1	1	20
Bronchiolitis	29	7	4	4	–	1	1	–	–	17
Croup	4	–	–	–	–	–	–	–	–	–
Tracheobronchitis	3	–	–	1	1	–	–	–	–	2
Total	83	13	8	9	4	2	1	1	1	39

RSV : Respiratory syncytial virus.
Para 1 : Parainfluenza type 1 virus.
Adenov: Adenoviruses.
MP : Mycoplasma pneumoniae.
Inf A : Influenza A virus.
Inf B : Influenza B virus.

Discussion

Mortality from acute lower respiratory disease is a serious problem in children under five years of age. Most children with respiratory tract illnesses are frequently seen in primary care clinics. Although minor upper respiratory tract infections are very common in childhood, they are not life-threatening for well-nourished children since death rates resulting from respiratory illnesses are closely linked to malnutrition. A study in Costa Rica showed that deaths resulting from bronchopneumonia in malnourished children are 12 times greater than in nourished children[1].

According to a study carried out in 1979 in Turkey, pneumonia was found to be the major cause of death in children in the 1-4 year age group[4]. In this age group, 31% of all deaths resulted from pneumonia[5]. The results of serologic studies in our study are consistent with the results of many other studies. In a WHO[6] study on respiratory ailments in children, 41 percent of patients developed a serological response to one or more of the agents we had investigated. Although this study was conducted in various countries, the results are similar to ours. Ong et al[7] reported that 32.6 percent of Malaysian children with respiratory infections exhibited serological evidence of infection with one or more of the same agents.

RSV is known as a major viral pathogen of respiratory tract diseases in children, especially in infections such as pneumonia and bronchiolitis in young infants. The disease may follow a fatal course in high risk infants such as those with congenital heart disease and bronchopulmonary dysplasia[8].

In our study serological evidence of RSV infection was found in 15.6 percent of patients. This agent was associated with 12.7 percent of pneumonia patients and 24 percent of bronchiolitis patients.

A study involving 662 children under three years of age hospitalized in Uganda showed that RSV was the pathogen which caused the lower respiratory tract infections in 17 percent of patients[9]. RSV infections were found to be present in 11 percent of 53 patients under two years of age, who had been hospitalized for bronchiolitis in Lagos, Nigeria[10].

RSV infections were associated with lower respiratory tract illnesses in about half of the patients we studied who were under one year of age.

The failure to detect an antibody rise to RSV in young infants using the complement-fixation technique has been previously reported[11], and, therefore, the exact value may actually be higher than what we found. Adenovirus infection was detected in 10.8 percent of the study group; five of these patients were in the 1-3 year age-group. Adenovirus infections account for 2-5 percent of all respiratory illnesses in children[12].

Parainfluenza virus Type 1 was detected in 9.6 percent of patients, and half of them were clinically diagnosed as having pneumonia and the rest as having bronchiolitis. Although parainfluenza virus Type 1 is the predominant agent associated with croup[13], it was not detected in our patients, probably because of the minimal number of patients with croup.

Influenza viruses were detected in five of our patients, two of whom also had other viruses. A patient infected with influenza A virus and parainfluenza virus Type 1 was clinically diagnosed as having pneumonia. This patient showed no improvement and died in three months.

Several aspects of respiratory disease due to *Mycoplasma pneumoniae* are different from those caused by viral pathogens[2]. *Mycoplasma pneumoniae* generally causes respiratory infections in children between the ages of 5-15[14]. Nagayama et al[15], demonstrated by using serological and isolation procedures that *Mycoplasma pneumoniae* infections occur frequently in young children. In this study, *Mycoplasma pneumoniae* was found to cause lower respiratory infections in 6.6 percent of children in the 0-2 year age-group and in 23.3 percent of children in the 3-6 year age-group.

We detected *Mycoplasma pneumoniae* infections in four patients, three of whom were diagnosed as having pneumonia and one as having tracheobronchitis. A WHO[7] study showed that 5 percent of pneumonias were caused by *Mycoplasma pneumoniae.*

Lower respiratory tract infections are common in young children, and decrease with age. Sixty-eight and a half percent of our patients were under three years of age and approximately 90 percent of these children who had bronchiolitis were under three years of age.

Pneumonia was seen in all age groups. Denny and Clyde[16] reported that the age - specific attack rate peak for pneumonia was reached between 3 - 5 years of age; tracheobronchitis occurred more frequently in the first two years of life, and the highest age - specific attack rates for bronchiolitis were seen in the second six months of life and for croup in the second year of life.

Wheezing, a common manifestation of acute respiratory illness in children was found in 24 percent of all patients and in 69 percent of patients with bronchiolitis. RSV has been reported to be the most common cause of wheezing associated with respiratory infections[17]. Wheezing was found in all seven RSV related-patients with bronchiolitis we studied.

Two agents were detected in the sera of two of our patients concomitantly. In respiratory diseases associated with significant rises in antibody titers to multiple agents, the increases may be due to simultaneous or sequential infections with two or more viruses occurring immediately before or during the period of time encompassed by the paired sera samples[18]. Simultaneous increases in titer may also be due to antigenic cross reactions among related agents, e.g., parainfluenza virus and mumps virus. In a study. Hilleman et al[19] showed 5 percent serologic responses to two agents.

Group A beta - hemolytic streptococci was isolated in the throat cultures of seven patients. In five of these patients, viruses were also detected. The association of viruses with group A streptococci has been reported in other studies[2].

An etiological agent could not be detected in 53 percent of our patients We believe that these patients were infected by other viruses or bacteria and that the agents under study in this paper could not be isolated because of the method used. Göçmen and Baki[20] have shown that some bacterial agents were the cause of pulmonary infections in 54.8 percent of 31 patients studied at Hacettepe University Children's Hospital.

Our patients will be followed for long - term complications of childhood lower respiratory tract infections because these infections, especially bronchiolitis, may lead to recurrent respiratory problems in subsequent years[21].

The results of this study suggest that various viruses are the major causes of lower respiratory tract infections in children in our region.

REFERENCES

1. Berman S, McIntosh K. Selective primary health care: strategies for control of disease in the developing world. XXI. Acute respiratory infections. *Rev Infect Dis* 7:674, 1985.
2. Loda FA, Clyde WA Jr, Glezen WP, et al. Studies on the role of viruses, bacteria, and M.pneumoniae as causes of lower respiratory tract infections in children. *J Pediatr* 72:161, 1968.
3. Grist NR, Bell EJ, Follett NC, Urguhort GE. *Diagnostic Methods In Clinical Virology* (3rd ed). Oxford: Blackwell Sci 1979, pp 95-115.
4. Distribution of 20 selected causes of death by age group in province and district centers (1986). *The First Interim Report of the Turkish State Planning Organization Health Sector Master Plan Study*, Ankara, 1989.
5. Egemen A, Enünlü T. Akut solunum yolu enfeksiyonlarının görülme sıklığı ve bunu etkileyen faktörler. UNESCO Raporu, Hacettepe Üniversitesi Halk Sağlığı Anabilim Dalı çalışmalarından, Ankara, 1989.
6. Chanock R, Chambon L, Chang W, et al. WHO respiratory disease survey in children: a serological study. *Bull WHO* 37:363, 1967.
7. Ong SB, Lam KL, Lam SK. Respiratory virus disease in Malaysian children: a serological study. *Bull WHO* 52:376, 1975.
8. Chiba S, Chiba Y, Numazaki K, et al. Pulmonary infections with respiratory syncytial virus and Chlamydia trachomatis in early infancy. *Acta Paediatr Jpn* Overseas *Ed* 30:225, 1988.
9. Soběslavský O, Sebikari SR, Harland PS, et al. The viral etiology of acute respiratory infections in children in Uganda. *Bull WHO* 55:625, 1977.
10. Ogunbi O. Bacteriological and viral aetiology of bronchiolitis and bronchopneumonia in Lagos children. *J Trop Med Hyg* 73:138, 1970.
11. Parrott RH, Vargosko AJ, Kim HW, et al. Respiratory syncytial virus. II. Serological studies over a 34-month period of children with bronchiolitis, pneumonia, and minor respiratory diseases. *JAMA* 176:653, 1961.
12. Pacini DL, Collier AM, Henderson FW. Adenovirus infections and respiratory illnesses in children in group day care. *J Infect Dis* 156:920, 1987.
13. Glezen WP, Denny FW. Epidemiology of acute lower respiratory disease in children. *N Engl J Med* 288:498, 1973.
14. Foy HM, Kenny GE, Cooney MK, Allan ID. Long-term epidemiology of infections with Mycoplasma pneumoniae. *J Infect Dis* 139:681, 1979.
15. Nagayama Y, Sakurai N, Yamamoto K, et al. Isolation of mycoplasma pneumoniae from children with lower-respiratory-tract infections. *J Infect Dis* 157:911, 1988.
16. Denny FW, Clyde WA Jr. Acute lower respiratory tract infections in nonhospitalized children. *J Pediatr* 108:635, 1986.
17. Henderson FW, Clyde WA Jr, Collier AM, et al. The etiologic and epidemiologic spectrum of bronchiolitis in pediatric practice. *J Pediatr* 95:183, 1979.
18. Portnoy B, Eckert HI, Hanes B, Salvatore MA. Multiple respiratory virus infections in hospitalized children. *Am J Epidemiol* 82:262, 1965.
19. Hilleman MR, Hamparian VV, Ketler H, et al. Acute respiratory illnesses among children and adults. Field study of contemporary importance of several viruses and appraisal of the literature. *JAMA* 180:445, 1962.
20. Göçmen A, Baki A. Çocukluk çağı akciğer enfeksiyonlarının etyolojik tanısında akciğer ponksiyonunun yeri. *Solunum* 3:134, 1980.
21. Burrows B, Knudson RJ, Lebowitz MD. The relationship of childhood respiratory illness to adult obstructive airway disease. *Am Rev Resp Dis* 115:751, 1977.