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ORIGINAL ARTICLE
ORİJİNAL ARAŞTIRMA

Clinical, Radiological, and Epidemiological Evaluation of Lower Respiratory Tract Infections of Children

Çocukluk Çağı Alt Solunum Yolu Enfeksiyonlarının Klinik, Radyolojik ve Epidemiyolojik Değerlendirmesi

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Abstract

Aim: In this study, we aimed to determine the etiology of lower respiratory tract infection in patients aged 1 month to 5 years with a clinical, radiological, and epidemiological study.

Material and Method: We investigated 150 patients between 1 month to 5 years of age who required hospitalization and those who were admitted to pediatrics clinics and pediatric emergency services of our center who had the clinical diagnosis of lower respiratory tract infection. Blood samples for acute phase reactants and nasopharyngeal swap samples for detection of bacterial etiologies were taken. Initial posteroanterior chest X-rays of all patients were checked.

Results: The most common pathogens were *Streptococcus pneumoniae* in 77 (51.3%) and *Haemophilus influenzae* in 71 (47.3%) patients. Three groups of patients compared with C-reactive protein values; patients with alveolar pneumonia were statistically higher than interstitial infiltrates (P=0.008). Erythrocyte sedimentation rates in patients with alveolar pneumonia were statistically significantly higher than the patients with interstitial infiltrates pneumonia (P=0.016).

Conclusion: In patients suspected of lower respiratory tract infection, the beginning of appropriate antibiotic treatment should be supported with clinical, radiological, and laboratory tests. We think laboratory tests of acute phase reactants should be used with multiplex PCR to detect viral and bacterial agents. Still, to deal with this issue, advanced studies are needed.

Keywords: Pneumonia, pediatrics, polymerase chain reaction

Öz

Amaç: Bu çalışmada alt solunum yolu enfeksiyonu klinik tanısıyla hastaneye yatırılan 1 ay-5 yaş arası hastalarda klinik, radyolojik ve epidemiyolojik çalışma ile etiyolojinin belirlenmesi amaçlandı.

Gereç ve Yöntem: Merkezimizin poliklinikleri ve çocuk acil servislerine başvuran, 1 ay-5 yaş arası, ASYE tanısı alan 150 hastayı inceledik. Akut faz reaktanları için kan örnekleri ve bakteriyel etiyolojilerin tespiti için nazofarengeal swap örnekleri alındı. Tüm hastaların ilk postero-anterior akciğer grafileri kontrol edildi.

Bulgular: En sık görülen patojenler 77 (51,3%) hastada *Streptococcus pneumoniae* ve 71 (47,3%) hastada *Haemophilus influenzae* idi. İki grup hasta C-reaktif protein değerleri açısından karşılaştırıldı; alveolar pnömonili hastalar interstisyel infiltrasyonu olan hasta grubundan istatistiksel olarak daha fazla idi (P=0.008). Alveoler pnömonili hastalarda eritrosit sedimantasyon hızı, interstisyel infiltrasyonu olan hastalara göre istatistiksel olarak anlamlı derecede yüksekti (P=0.016).

Sonuç: Alt solunum yolu enfeksiyonu şüphesi olan hastalarda uygun antibiyotik tedavisine başlanması klinik, radyolojik ve laboratuvar tetkikleriyle desteklenmelidir. Viral ve bakteriyel etkenlerin saptanmasında laboratuvar testlerinin multipleks polimeraz zincir reaksiyonu yöntemiyle birlikte kullanılabileceğini ancak bu konuyla ilgili ileri çalışmalara ihtiyaç olduğunu düşünüyoruz.

Anahtar Kelimeler: Pnömoni, çocuk sağlığı, polimeraz zincir reaksiyonu

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INTRODUCTION

Lower respiratory tract infection (LRTI) is the most critical disease and mortality caused in infancy, especially in developing countries. According to the World Health Organization, LRTI is responsible for about 20% of annual 10 million deaths under the age of 5 (1,2). According to the Turkey Disease Load Study carried out by the Ministry of Health of Turkey between the years 2002 and 2004, LRTI is the second most frequent cause of death in the age group of 0-4 years (13.4%) and those of 5-14 years (6.5%). The same study also shows LRTI is solely responsible for 14% of total deaths in the 0-14 (3,4).

Determination of the agent in a patient with the community–acquired LRTI leads to the administration of correct antibiotics. This is important because it will allow the selection of narrower-spectrum antibiotics, ultimately leading to fewer side effects and less development of resistance. This study aimed to determine the etiology in patients aged 1 month-5 years hospitalized with the clinical diagnosis of LRTI with clinical, radiological, acute phase reactants, blood cultures, and nasopharyngeal swaps with polymerase chain reaction (PCR).

MATERIAL AND METHOD

Study Groups

A group of 150 patients between the ages of 1 month and 5 years with clinical LRTI diagnosis were addmission to the Pediatrics Department of our center. They did not use any antibiotics at least 48 hours before admission.

The informed consent of the families was also obtained. The study then carried on for six months between 1 February 2011 and 1 August 2011.

To exclude hospital-acquired pneumonia, the patients who had stayed in the hospital previously were excluded if at least two weeks had not passed since their discharge. Moreover, lower respiratory tract infection patients with chronic diseases like asthma, congenital heart disease, and malnutrition were also excluded from the study.

The lower respiratory tract infection was diagnosed upon clinical signs and symptoms and/or upon detection of infiltrations in chest x-rays. Clinically, fever and acute respiratory symptoms were sought in patients. For diagnosing pneumonia, the tachypnea criteria defined by WHO by age were used (5).

The information of children included in the study on the date of their application, age, gender, place of residence, status of immunization, any previous hospitalization due to lower respiratory tract infection, exposure to smoking habits and all symptoms of them were questioned and recorded. Also, vital findings of the patients at the time of application, their respiratory rates per minute and other physical examination findings like chest wall retraction, rales, and rhonchus were recorded. Blood samples were collected from all patients for complete blood count, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), procalcitonin (PKT) tests and blood culture. All blood samples were analyzed in the laboratory of our center.

Samples

Collection and conservation of samples: The nasopharyngeal swab samples for PCR analysis for *Streptococcus pneumonia*, *Mycoplasma pneumonia*, *Haemophilus influenzae*, *Chlamydia pneumonia*, *Bordetella pertussis*, *Legionella pneumophilia* were collected from patients by averages of nasopharyngeal swabs. The samples were preserved at -70 C until the PCR was applied.

Isolation of DNA from samples: For isolating nucleic acids from nasal swap, a QIAamp DNA Mini Kit (Cat. No. 51304, QIAGEN, Germany) was used.

Interpretation of radiologic inspections: All the patients included in the study were subjected to postero-anterior chest radiography at their admission to the hospital. The radiological findings were classified as interstitial infiltration, peribronchial thickening, hilar enlargement, atelectasis, increased aeration, pleural effusion and alveolar consolidation. The localization of each finding on the lungs was recorded. The same radiology specialist interpreted all the graphs.

Statistical Analysis

For analyzing the data, the SPSS 17.0 statistics package program was used. Average, standard deviation, median, lower limits and upper limit criteria were defined for constant variables like age, respiratory rate and laboratory work values. According to the distribution of these variables by their comparison with the groups, if the distribution is normal, a t-test or one–way analysis of variance in independent groups, and if the distribution is not normal, Mann Whitney U test or Kruskal Wallis test was used. For categorical variables like gender or physical examination findings, counts and percentage criteria were given. The chi-square test was utilized for comparing these in groups. In all analyses, the level of statistical significance was taken as $p < 0.05$.

The study protocol was approved by the Clinical Research Ethics Committee of our center (Decision dated 26th January 2011, numbered 402/3357).

RESULTS

Demographic and Clinical Characteristics of Patients

In this study, 150 children patients with LRTI diagnosis were included. The demographic characteristics of the patients are shown in **Table 1**.

Table 1: Demographical characteristics of patients	
Demographical characteristics	
Age (mounth)	
Mean (± SD)	18,78 ±15,71
Sex (%)	
Male	92 (61,3)
Female	58 (38.7)
Immunization (%)	
Fully immunized by age	148(98.7)
Previus hospitalization for LRTI	46(30)
Smoking in the family	63 (42)

The most frequent symptom of patients was cough 122 (98.9%); then nasal discharge 88 (58.7%), wheezing 84 (56%), nasal congestion 81 (54%), respiratory distress 77 (51%), fever 71 (47.3%), irritability 64 (42.7%), lack of appetite 73 (49%), vomiting 53 (35.3%), cyanosis 40 (26.7%), chest pain 5 (3.3%) and abdominal pain 13 (8.7%).

The most common findings on physical examination was tachypnea 123 (82%), rhonchus 109 (72.7%), retraction 103 (68.7%) and rales 99 (66%).

Microbiological findings detected in patients are listed in **Table 2**.

Table 2: Microbiological findings of patients.	
Agent	**Patient n(%)**
Bacteria detected in nasopharyngeal swap	
M. pneumonia	2 (1.3)
L. pneumophilia	0 (0)
S. pneumonia	77 (51)
H. influenzae	71 (47)
B. pertussis	6 (4.0)
C. pneumonia	8 (5.3)
Detection of several bacteria in nasopharyngeal swap	
M. pneumonia+S. pneumonia	1 (0.7)
M. pneumonia+H. influenzae	1 (0.7)
S. pneumonia +H. influenzae	39 (26)
S. pneumonia+B. pertussis	1 (0.7)
S. pneumonia+C. pneumonia	1 (0.7)
H. influenzae +B. pertussis	4 (2.7)
H. influenzae +C. pneumonia	5 (3.3)
B. pertussis+C. pneumonia	3 (2)

Radiological Characteristics of Patients

When the PA lung radiographs taken at the time of admission of the patients included in the study were evaluated, pneumonia was not detected in 38 patients (25.3%), alveolar pneumonia was detected in 7 patients (7%), and interstitial pneumonia was detected in 105 patients. There were signs of interstitial pneumonia (70%), hilar enlargement in 8 patients (5.3%), and hyperinflation in 11 patients (7.3%). Neither atelectasis nor pleural effusion were determined in any of the patients.

Clinical Characteristics of Patients According to Etiologic Agents

Among symptoms, lack of appetite (P=0.05) was more frequent in the patient group that showed *Streptococcus pneumonia*, while fever (P=0.03), chest pain (P=0.02), and respiratory distress (P=0.01) were a more frequent patient group of *Haemophilus influenzae*; and cyanosis (P=0.04) and irritability (P=0.05) were most frequent in *Bordetella pertussis* group.

Among physical examination findings, the rhonchus was more frequent in the *Streptococcus pneumonia* patient group (P=0.04), while fever was more frequent (P=0.03) in the patient group of *Haemophilus influenzae* was detected.

Among acute phase reactants, CRP (P=0.053) and PCT (P=0.042) were detected highest in the *Haemophilus influenzae* patient group. No significant difference was detected between white blood cell count, absolute neutrophil count and ESR levels. (**Table 3**).

Among radiologic findings, interstitial infiltration and hyper aeration were more frequent in patients with *Haemophilus influenzae* (P=0.03, P=0.02).

Clinical and radiological characteristics of patient groups of no pneumonia, alveolar pneumonia and interstitial pneumonia

Among symptoms, fever was detected as significantly higher in the patient group of interstitial infiltration than in the patient group with normal radiography results (P=0.031). On the other hand, abdominal pain (P=0.017, P=0.035), lack of appetite (P=0.005, P=0.029) and vomiting (P=0.01, P=0.001) in the patient group of alveolar pneumonia were determined to be significantly higher as compared to both the patient group with normal radiography results and to the patient group in which interstitial infiltration was detected.

When physical examination findings are compared, the fever was significantly higher in the alveolar pneumonia group compared to both the patient group with normal radiography results and to the patient group in which interstitial infiltration was detected (P=0.039, P=0.022).

A comparison of acute phase reactants of three patient groups is listed in **Table 4**.

Table 3: Acute phase reactants according to the agent.

	Streptococcus pneumonia	P	*Haemophilus influenzae*	P	*Bordetella pertussis*	P	*Chlamydia pneumonia*	P
White blood cell count (×10^9/L) (average±SD)	13.4±4.7	0.110	13.4±5.4	0.264	12.9±4.5	0.867	14.6±6.1	0.389
Median	13.1		12.1		12.7		12.9	
Lower-upper limit	4.8-28.5		3.8-31.3		8-18.4		8-26.9	
Absolute neutrophile count (×10^9/L) (average±SD)	11.2±4.5	0.084	12.3±4.4	0.346	11.1±51.2	0.726	14.3±4	0.123
Median	11		12		11.2		13.1	
Lower-upper limit	2.3-20.5		3.4-21.5		3.7- 18.9		9.3-18.9	
C-reactive protein (mg/L) (average±SD)	2.55±5.68	0.062	2.83±5.7	0.053	1.83±2.97	0.536	2.91±4.42	0.880
Median	1.36		1.31		0.34		0.74	
Lower-upper limit	0.10-46.7		0.1-46.7		0.20-7.73		0.20-11.9	
Procalcitonin (ng/ml) (average±SD)	0.30±0.67	0.729	0.42±0.82	0.042	0.15±0.12	0.430	0.21±0.13	0.455
Median	0.10		0.10		0.10		0.10	
Lower-upper limit	0.07-4.43		0.10-4.43		0.1-0.41		0.10-0.41	
Erythrocyte sedimentation rate (mm/h) (average±SD)	26.45±5.6	0.630	29.43±26	0.147	32± 22	0.645	30± 17	0.513
Median	21		23		21		25	
Lower-upper limit	2-120		2-120		11-75		12-58	

Table 4: Acute phase reactants of those patient groups of non-radiologically pneumonia detection, with alveolar pneumonia and with interstitial pneumonia

	With normal radiology	Alveolar pneumonia	Interstitial pneumonia	P
White blood cell count (×10^9/L)				0.359
(Average±SD)	12.6± 4.7	14±6.7	12.8±4	
median (lower-upper limit)	11.9 (6.1-28.5)	17.2(3.3-22.9)	12.3(3.8-31.3)	
Absolute neutrophile count (×10^9/L)				0.517
(Average±SD)	11.7±5	13.8±3.7	11.9±4.6	
median (lower-upper limit)	11.1 (3-21.3)	13.4 (9.5-18.8)	11.5	
C-reactive protein (mg/L)				0.028
(Average±SD)	1.91± 2.66	6.16± 5.09	2.17± 4.74	
median (lower-upper limit)	0.77 (0.1-11.9)	6.41 (1.04–14.2)	1.07 (0.1-46.7)	
Procalcitonin (ng/ml)				0.452
(Average±SD)	0.38±0.63	0.23± 0.15	0.30± 0.60	
median (lower-upper limit)	0.10 (0.10-4.43)	0.14 (0.10-0.45)	0.10 (0.44-3.95)	
Erythrocyte sedimentation rate (mm/h)				0.049
(Average±SD)	21.8± 17.1	45.8± 29.8	26.1± 23.2	
median (lower-upper limit)	21 (2-64)	35 (22-95)	20.5 (2-120)	

DISCUSSION

In developing countries, a total of 23% of pediatric age group patients are treated as outpatients and a total of 29-38% hospitalized pediatric age group patients are diagnosed with pneumonia (5). According to 2002 data from Turkish Toraks Association, the LRTI frequency in Turkey in between 0-1 ages is 30-35% (5). In our study, a large part of our patients was constituted of patients under the age of 12 months. In parallel to previous publications, our research found a relation between the underage, especially under the age of 12 months, and the higher hospitalization rates (6).

In our study, the most frequent complaints, in descending order by frequency, were cough (81.3%), respiratory distress (63.7%), and nasal congestion (58.7%). The most frequent symptom detected in our study was fever (which is in parallel with the literature). However, the frequency of tachypnea in our study was higher than in the literature (7-9).

In our study, among a total of 150 patients, rales was detected in 99 patients (66%); tachypnea in 123 patients (82%); rhonchus in 109 patients (72.7%), and chest wall retraction in 103 of patients (68.7%). According to previous studies, abnormal listening was detected in most of our study (8, 9, 10).

In previous publications, tachypnoea has been reported in 50-80% of radiologically confirmed cases of childhood LRTI (11). The sensitivity of tachypnea existence in indicating pneumonia is 50-81%, while its selectivity is 54-70% (12,13). On the other hand, the sensitivity of rales existence for diagnosing pneumonia is 43-76% (14,15). In a study conducted by Bilkis et al. (16) in 2010, it is

reported that their sensitivity in indicating pneumonia for children with both fevers, localized rales, decreased respiratory sounds, and tachypnea is 93.8%. Similarly, in our study, the frequency of tachypnea was by the literature, while the frequency of the rales was higher than those reported in the literature.

Different methods for determining etiological factors are employed in such studies in which children hospitalized with a diagnosis of lower respiratory tract infections are included. For this reason, the frequency of etiological factors is reported with different rates. In prospective studies in which standard diagnostic methods are used, the factor detection rate of children with LRTI varies between 42% and 85% (17).

In our study, among 150 patients, at least one bacteria was found in a nasopharyngeal swap of 106 patients (70%) and several bacterial factors were found in 55 patients (36.6%) via multiplex PCR method. No factor was detected in 44 patients (29%) through the multiplex PCR method. In descending order by frequency, *Haemophilus influenzae* in 77 patients (51.3%), *Streptococcus pneumonia* in 71 patients (47.3%), and *Chlamydia pneumonia* in 8 patients (5.3%) were detected. In our study, *Streptococcus pneumonia* is the most frequent bacterial factor, also in line with many previous publications (7, 18-24)

No interstitial pneumonia was observed on radiological examination in 105 patients (70 %), while 38 patients (25.3 %) had no evidence of pneumonia. However, in 7 patients (4.7%), alveolar pneumonia was detected radiological. When radiologic findings are analyzed, in 11 patients (7.3%), hyper aeration in 8 patients (5.3%), hilar enlargement is detected. No pleural effusion and atelectasis are detected in any patient. In our study, radiological pneumonia detection rates are higher than Hazır et al. (25) reported. Virkki et al. (24) determined 22% alveolar changes, 39% interstitial changes, and 39% combinations of alveolar interstitial changes in their study. Our study's most consistent radiological finding in previous publications is interstitial infiltration (24, 26).

When radiological findings of our study are compared with the factors, interstitial infiltration and hyper aeration are observed more frequently in patients in which *Haemophilus influenzae* is detected. In the past, in many studies, no finding that proves the existence of bacterial pneumonia through radiological averages was determined (24). When Turner et al. (27) radiologically assessed 37 patients with pneumonia the alveolar infiltration was observed in 38% of patients with bacterial pneumonia, while it was kept in 67% of those with viral pneumonia. Courtoy et al. (28) observed alveolar infiltration in 67% of 24 patients with viral pneumonia and 42% of 12 patients with bacterial pneumonia. There was no difference in the distribution of etiologic factors between the radiologically confirmed cases of pneumonia and the groups for which pneumonia was not detected radiologically (29).

In our study, the procalcitonin and C-reactive proteins are found in high levels in patients with *Haemophilus influenzae*. Madhi et al. (20) also determined that a high C-reactive protein level alone is more beneficial than a clinical diagnosis in differentiating bacterial cases of pneumonia. However, Korppi et al. (29) could not prove the efficiency of any clinical or radiological data in determining LRTI etiology.

In our study, *Haemophilus influenzae*, as a factor of pneumonia, was detected in 51% of children vaccinated (98.3%) against type b *Haemophilus influenzae*. However, separation of the *Haemophilus influenzae* serotype could not be performed. In the study conducted by Campos et al. (30), it is stated that the number of type b *Haemophilus influenzae* invasive infections is reduced upon effective vaccination yet that the frequency of diseases of non–type b serotypes of *Haemophilus influenzae* is increased as a factor in otitis media and LRTI.

CONCLUSION

As a result, our study assessed the epidemiological, clinical, and radiological characteristics and bacterial factors in children with LRTI diagnosis at the age of 1 month to 5 years. The most frequent bacterial factor was *Streptococcus pneumonia*. For patients suspected of LRTI to start appropriate antibiotic treatment, the diagnosis must be supported with clinical, laboratory tests and/or radiological. In our opinion, the multiplex PCR method must be used in conjunction with acute phase reactants for laboratory tests. We believe that, regarding this issue, more advanced-level studies examining both viral and bacterial factors together are required.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study protocol was approved by the Clinical Research Ethics Committee of the Ankara Training and Research Hospital (Decision dated 26th January 2011, numbered 402/3357)

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

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