Risk Factors for the Development of Community-Acquired Pneumonia in Young Adults*

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Abstract

Background: Community-acquired pneumonia (CAP) is a common and severe illness. The factors thought to predispose to development of CAP in young patients have not previously been reported. We, therefore, conducted a retrospective case-control study to assess the risk factors and the clinical aspects of CAP in young adult patients.

Methods: We studied fifty-six patients (age <40 years) who were seen in both a university hospital and a community hospital from January 1995 to November 1998. They were matched by sex and age with fifty-six control subjects. The diagnostic criteria for CAP were based on clinical and radiological findings. Patients with human immunodeficiency virus infection, transplant recipients, those with neoplasia or autoimmune disorders, and those treated with high doses corticosteroids were excluded. Risk factors including habits, medical history, physical examination and radiographical findings, laboratory data and treatments were recorded.

Results: The mean age was 29 years (range, 16 to 40 years). Etiological diagnosis was achieved in 12 patients (21.4%): 8 *S. pneumoniae* (7 in sputum and 1 in pleural fluid), 3 *L. pneumophila* and 1 *M. pneumoniae*. Lobar consolidation was the most prevalent radiographical presentation and extrapulmonary symptoms were seen in 36% of the patients. In the univariate analysis, an increased risk of CAP was associated with ex and current smoking, hypoalbuminemia, previous pneumonia or recent respiratory infection. In the multivariate analysis, the only statistically significant risk factor for CAP was ex and current smoking (Odds ratio=2.5; 95% confidence interval 1.02-6.43, p=0.046).

Conlusions: This study revealed that smoking is the most important risk factor for CAP in young adults. Preventive measures will reduce the risk of pneumonia in this age group.

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Key words: *Risk factors, community-acquired pneumonia, young patients*

Introduction

Community-acquired pneumonia (CAP) remains a common and persistant cause of morbidity and mortality. Despite the development of multiple new antimicrobials, there is little evidence to document that either the incidence or morbidity of pneumonia has declined over the last 30 years. The overall attack rate is about 12 cases per 1000 persons annually (1). The attack rates are the highest at the extreme ages. Pneumonia is the sixth leading cause of death in the United States, with an estimated 4 million cases annually (1).

Aging, alcoholism, dementia, seizures, previous pneumonia, smoking, malnutrition and the presence of chronic illnesses such as chronic obstructive pulmonary disease, chronic liver and kidney disease, congestive heart failure, diabetes and

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cerebrovascular disease have been identified as significant risk factors for the development of pneumonia in middle-aged or older people (2-11). However, the risk factors in young adults have not previously been reported.

The aim of the present study was therefore, to assess the risk factors associated with the development of CAP in patients younger than 40 years and the clinical characteristics of these patients.

Patients and Methods

Between January 1995 and November 1998, we studied 63 young adult patients, ages over 16 but under 40 years, seen consecutively in a 600-bed university hospital and a 650-bed community hospital (Akdeniz University Hospital and Antalya State Hospital, Antalya) because of community-acquired pneumonia. Patients from various socioeconomic strata are seen in these hospitals. The pulmonary clinics are staffed by pulmonary specialists and residents. Patients attending these clinics typically have predominantly pulmonary problems. Complete documentation was available for 56 of the 63 patients. Patients with HIV, transplant recipients, those with neoplasia or autoimmune disorders, and those treated with high doses corticosteroids (>20 mg/d of prednisone) were excluded. A control group was composed of 56 patients matched by age (±3 yrs) and sex with the patients with pneumonia. All were randomly selected among the patients seen in the outpatient clinic of respiratory disease and who fullfilled the same criteria as the cases, except that they did not have pneumonia. The diagnostic criteria for CAP were based on clinical and radiological findings: cough with or without sputum production, fever (temperature >38°C), leukocytosis or leukopenia and pulmonary infiltrates on the chest x-ray obtained on admission to the hospital. Patients were managed according to the decisions of the attending physician.

The following information was recorded in all patients and controls: age, sex, underlying disease, alcohol consumption, smoking habit, laboratory tests, including hemoglobin level, and levels of total protein, albumin, serum aspartate (AST), alanine aminotransferase (ALT) and lactate dehydrogenase (ALT). Red blood cell, white blood cell, platelet counts and erythrocyte sedimentation rate (ESR) were performed. We also examined the clinical presentation on admission for fever, pleuritic pain, cough, sputum production, dyspnea and extrapulmonary symptoms such as headache, myalgia, arthralgia and gastrointestinal symptoms. The physical examination included the presence or absence of crepitations, diminished breath sounds, bronchial breathing and rhonchi on auscultation. Radiographical infiltrates were evaluated as lobar, segmental or interstitial and the presence of accompanying findings such as pleural effusion, cavitation and hilar adenopathy were also noted.

A definitive diagnosis of the etiological agent was made when either the blood cultures or the pleural fluid cultures were positive. A four-fold rise in mycoplasma serology or a single titre of 1:256 or higher in the *Mycoplasma* spesific to IgG immunofluorescent antibody test, was considered as an evidence of *Mycoplasma* infection. The DFA examination of respiratory tract secretion established a diagnosis of *Legionella* infection. A probable diagnosis was also made when sputum or endotracheal aspirate culture were positive. Sputum samples could not be obtained from 29 patients.

High alcohol intake was considered to be present when daily alcohol consumption was higher than 100 g for men and 80 g for women during at least two years before admission. A patient was considered a smoker if he or she reported active consumption of more than 10 pack-years. Hypoalbuminemia was described if the serum level of albumin was less than 3.5 g/dL.

For the comparison of means, we used the nonparametric Mann-Whitney U test for continuous variables that departed from a normal distribution. Otherwise, we used Student's *t* test and the chi-square test for discrete data. As a measure of association between the risk factors and the occurrence of CAP, estimations of the relative risk through odds ratios (OR) were used. These were calculated using conditional logistic regression and presented with 95% confidence intervals. All variables were first univariately analysed and only those close to statistical significance ($p<0.05$) were used to fit a multivariate model.

Results

Fifty-six patients had pneumonia and were considered as cases, and an equal number without pneumonia were used as controls. The general characteristics and clinical findings of the cases are outlined in Table 1. The patients age was 29±8 year (mean ±SD) (range 16 to 40). The mean age of the control subjects was 29±4. Forty-five (80%) of the patients were treated at home and the remainder were admitted to the hospital. The most frequent underlying disease states in the pneumonia group were diabetes mellitus in 5 cases, asthma in 3 cases and cardiac disease in 2 cases. There were no significant dif-

Table 1. General characteristics and clinical findings of the study population (n=56)

Age, yr*	29±8
Gender, M/F	35/21
Clinical symptoms	
Cough	41 (73%)
Sputum production	39 (69%)
Fever (>38°C)	37 (66%)
Pleuritic chest pain	11 (19%)
Dyspnea	8 (14%)
Extrapulmonary symptoms	20 (36%)
Underlying disease	
Diabetes mellitus	5 (9%)
Asthma	3 (5%)
Cardiac disease	2 (3%)
Radiographical patterns	
Lobar pneumonia	44 (78%)
Bronchopneumonia	10 (18%)
Interstitial pneumonia	2 (4%)
Pleural effusion	8 (14%)
Bilateral infiltrates	5 (9%)
Cavitation	1 (2%)

* Mean SD

ferences between the groups in terms of underlying diseases. The main presentations were cough in 41 (73%) patients, sputum production in 39 (69%) patients and fever in 37 (66%) patients. Extrapulmonary symptoms were seen in 20 (36%) patients. The chest radiographical infiltrate pattern on admission was lobar in most of the cases (78%). There were 8 (14%) patients whose pneumonic infiltration was associated with pleural effusion. Of these 8 patients, 1 had empyema and tube thoracostomy was performed. The other patients had "benign" parapneumonic exudates.

Thirty-three (59%) patients had a leukocyte count >10.000/mm^3. The most frequent auscultatory finding was crepitations in 46 (82%) cases. Three patients had normal auscultatory findings. Etiological diagnosis was achieved in 12 (21%) of the cases. The etiological agents were: *Streptococcus pneumoniae* 8 (14%) (7 in sputum and 1 in pleural fluid), *Legionella pneumophila* 3 (5%) and *Mycoplasma pneumoniae* 1 (2%). While 57% of the patients received macrolides alone, 32% of the patients received combination therapy.

Table 2. Laboratory findings of CAP patients and controls*

Variable	Cases (n=56)	Controls (n=56)	p Value
Hemoglobin	12.6±1.49	14.33±1.58	<0.001
Leukocyte count	14483.3±7629.58	7388.12±1871.89	<0.001
ESR (mm/h)	45.06±25.03	7.62±7.76	<0.001
Total protein (g/dL)	6.51±1.08	7.5±60.47	<0.001
Albumin (g/dL)	2.86±0.68	5.01±0.57	<0.001
ALT (U/L)	48.27±51.34	198.05	<0.001
AST (U/L)	49.66±62.37	20.96±6.99	<0.001
LDH (U/L)	280.82±150.90	249.25108.64	<0.001

Definition of abbreviations: ALT = alanine transaminase; AST = aspartate transaminase; LDH = lactat dehydrogenase
* Mean SD

Table 2 summarizes the differences in the biochemical profiles of the subjects with CAP and controls. CAP patients revealed higher levels of leukocyte, ESR, ALT, AST and LDH compared with the control group (p<0.001). However, the control subjects had higher levels of Hb, total protein and albumin (p<0.001).

For evaluating the risk factors associated with the development of pneumonia, a univariate analysis was used. Table 3 shows the variables with statistical significance. The presence of the following risk factors was more common in the cases than in the control subjects: ex and current smoking, hypoalbuminemia and previous pneumonia or recent respiratory infection. There were no differences as regards to the remaining variables. The

Table 3. Univariate analysis of the risk factors for developing CAP in young patients

Risk factor	Cases (n=56)	Controls (n=56)	OR	95% CI	p Value
Ex and current smoking	23	11	2.81	1.22-6.65	0.014
Hypoalbuminemia	24	–	–	–	<0.001
Previous pneumonia or recent respiratory infection	6	–	–	–	0.027
Alcoholism	1	–	–	–	0.614
Diabetes mellitus	5	1	5.39	0.60-47.72	0.216
Asthma	3	2	1.53	5-9.52	0.647
Cardiac disease	2	2	1	0.14-7.36	1

Definition of abbreviations: OR = odds ratio; CI = confidence interval.

multivariate analysis demonstrated that ex and current smoking was an independent risk factor significantly related to the development of pneumonia (OR=2.5; 95% confidence interval 1.02-6.43, p=0.046).

Discussion

Patients with acute CAP are usually in their mid-50s to late 60s. Most patients (58-89%) have one or more chronic underlying diseases, including chronic obstructive pulmonary disease (COPD), diabetes, cirrhosis, cardiac failure, asthma, dementia, cerebrovascular disease and renal failure (12). Immunosuppression including the presence of malignancy, neutropenia, or chronic use of steroids or myelosuppressive agents may be present in up to 36% of the patients (12). Several studies have been conducted to determine the risk factors for CAP and these factors have been clearly established in middle-aged or elderly people. To the best of our knowledge, there are no studies on the risk factors in young patients with CAP.

In the current case-control study, we have demonstrated that smoking, hypoalbuminemia, and previous pneumonia or recent respiratory infection were statistically significant risk factors for CAP in young adults. Other risk factors, such as alcoholism, diabetes mellitus, asthma or cardiac disease did not increase the risk for pneumonia in this population. Some investigators have shown that alcoholics are particularly prone to pneumonia and pneumococcal bacteriemia (13). In one study, it was shown that active high alcohol intake was the only independent risk and prognostic factor for CAP in middle-aged people (7). However, similar to the results of Almirall et al. (2) and Riquelme et al. (5), we have not found any association between alcoholism and pneumonia. Diabetes mellitus is regarded as a risk factor for developing infections because of hyperglicemia and ketosis, and patients with insulin-dependent diabetes mellitus have high influenza-associated morbidity and increased risk for pneumonia (14). Although diabetes mellitus was the most frequent underlying disease in our young population, it did not show a significant increase in risk.

We found that cigarette smoking was strongly associated with developing CAP. In the multivariate analysis, the only risk factor for CAP was cigarette smoking. It has been clearly established that the smoking rates in young Turkish population is high (15). In two comprehensive studies, it has been shown that as many as 54% of CAP cases had a smoking history (16,17). In one population based case-control study (18), a positive trend for increased risk of CAP was observed for an increase in the duration of the habit, the average number of cigarettes smoked daily, and cumulative cigarette consumption. In the same study (18), smoking had an odds ratio of CAP of 2 for patients with any history of smoking (1.88 for current smokers and 2.14 for ex-smokers). Several lines of evidence suggest that cigarette smoking alters the respiratory tract's ability to defend itself from infection (19). Ciliary function is impaired, mucous volume is increased, humoral response to antigens altered, and quantitative and qualitative changes in cellular components occur (19). Recently, Piatti et al. (20) have shown an increased pneumococcal adherence in smokers compared with that of non-smokers and this may explain the role of smoking as a risk factor in the susceptibility to bacterial pneumonia.

Malnutrition status has been associated with the risk of CAP, and the clinical degree of malnutrition correlates with morbidity and mortality in both young children and elderly people (21-26). It has been postulated that, in patients who are admitted to the hospital for CAP, a low serum albumin level on admission should warrant intensified observation and treatment (24). The effects of malnutrition in adults are not so clear. Severe protein deficiency has the most profound effect on cell-mediated immunity (27). The effects on humoral immunity are less clear (27). Albumin may not be the best parameter reflecting nutritional status. A drawback of our study is lack of other nutritional measurements such as weight, history of weight loss, body mass index, triceps skinfold thickness and mid-arm perimeter, because this information was not recorded in the file. In order to determine whether low serum albumin concentrations observed in young CAP patients reflect poor nutritional status, further prospective studies are needed.

A relevant risk factor found in our univariate analysis was the history of pneumonia or recent respiratory infection. Previous episode of pneumonia seems to be an important marker for increased risk of having new pneumonia. Recent viral infection may impair mucociliary clearence and predispose to *S. pneumoniae* and, rarely, *S. aureus* (28). Hedlund et al. (29) have shown that the risk of re-admission for pneumonia during 3 years after discharge was more than five times higher, if the initial diagnosis had been pneumonia than if it had been another infectious disease. More recently, Almirall et al. (2) reported that people with a previous diagnosis of pneumonia had a nearly two-fold higher risk of a subsequent CAP. In our series of 56 patients, 11% had a previous pneumonia episode or recent respiratory viral infection in our study.

As 80% of patients with pneumonia were treated on an ambulatory basis in our study, the causes of pneumonia had not been well studied. Other less likely explanation for the low percentage of microbiological eradication might be due to viral etiology. Lack of viral assessment is another limitation of this study. Any future prospective study should warrant viral assessment. Viral agents are detected in 2% to 15% of CAP cases (12). Viruses probably account for a substantial number of the pneumonia cases in our otherwise healthy young population.

Respiratory and nonrespiratory symptoms were frequently reported by our young patients with CAP and 82% of cases had abnormal physical findings on admission. The clinical presentation of CAP in elderly patients differs from that of CAP in young patients in some respects (30). The signs and symptoms and physical findings may be seen less commonly in older populations. The classical findings of cough, fever and dyspnea may be absent in over half of the elderly patients (20, 31) and the absence of fever and leukocytosis might be associated with poor prognosis in this age group (5, 32).

We conclude that smoking should be considered as the most important risk factor for the development of CAP in young people. Efforts to prevent smoking initiation and to encourage smoking cessation will be effective methods for reducing CAP incidence in this age group.

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