Turk Thorac J 2021; 22(4): 339-345 DOI: 10.5152/TurkThoracJ.2021.20223

Original Article

The Role of Pneumococcal Pneumonia among Community-Acquired Pneumonia in Adult Turkish Population: TurkCAP Study

Esin Şenol[1], Aykut Çilli[2], Hakan Günen[3], Alper Şener[4], Rıdvan Dumlu[4], Ayşe Ödemiş[2], Ayşe Füsun Topçu[5], Yeşim Yıldız[6], Rahmet Güner[7], Ayhan Özhasenekler[8], Birsen Mutlu[9], Nurdan Köktürk[10], Nurgül Sevimli[10], Nurcan Baykam[11], Derya Yapar[11], Selami Ekin[12], Mehmet Polatlı[13], Şebnem Eren Gök[14], Oğuz Kılınç[15], Abdullah Sayıner[16], Ömer Karaşahin[17], Çağlar Çuhadaroğlu[18], Ayşe Sesin Kocagöz[19], Turhan Togan[20], Hüseyin Arpağ[21], Hakan Katı[1], İftihar Köksal[22], Firdevs Aksoy[22], Canan Hasanoğlu[23]

[1]Department of Infectious Diseases, Gazi University, Faculty of Medicine, Ankara, Turkey
[2]Department of Pulmonary Diseases, Akdeniz University, Faculty of Medicine, Antalya, Turkey
[3]Department of Pulmonary Diseases, Süreyyapaşa Chest Diseases and Thoracic Surgery Training and Research Hospital, Istanbul, Turkey
[4]Department of Infectious Diseases and Clinical Microbiology, 18 Mart University, Faculty of Medicine, Çanakkale, Turkey
[5]Department of Pulmonary Diseases, Dicle University, Faculty of Medicine, Diyarbakır, Turkey
[6]Department of Infectious Diseases and Clinical Microbiology, Mardin State Hospital, Mardin, Turkey
[7]Department of Infectious Diseases and Clinical Microbiology, Ankara Atatürk Training and Research Hospital, Ankara, Turkey
[8]Department of Emergency Medicine, Ankara Atatürk Training and Research Hospital, Ankara, Turkey
[9]Department of Infectious Diseases, Kocaeli University, Faculty of Medicine, Kocaeli, Turkey
[10]Department of Pulmonary Diseases, Gazi University, Faculty of Medicine, Ankara, Turkey
[11]Department of Infectious Diseases and Clinical Microbiology, Hitit University, Faculty of Medicine, Çorum, Turkey
[12]Department of Pulmonary Diseases, Yüzüncü Yıl University, Faculty of Medicine, Van, Turkey
[13]Department of Pulmonary Diseases, Adnan Menderes University, Faculty of Medicine, Aydın, Turkey
[14]Department of Infectious Diseases and Clinical Microbiology, Bozok University, Faculty of Medicine, Yozgat, Turkey
[15]Department of Pulmonary Diseases, Dokuz Eylül University, Faculty of Medicine, Izmir, Turkey
[16]Department of Pulmonary Diseases, Ege University, Faculty of Medicine, Izmir, Turkey
[17]Department of Infectious Diseases and Clinical Microbiology, Erzurum Regional Training and Research Hospital, Erzurum, Turkey
[18]Department of Pulmonary Diseases and Sleep Disorder, Acıbadem Health Group Maslak Hospital, Istanbul, Turkey
[19]Department of Infectious Diseases and Clinical Microbiology, Acıbadem Health Group Maslak Hospital, Istanbul, Turkey
[20]Department of Infectious Diseases and Clinical Microbiology, Başkent University Konya Hospital, Konya, Turkey
[21]Department of Pulmonary Diseases, Sutcu Imam University, Faculty of Medicine, Kahramanmaraş, Turkey
[22]Department of Infectious Diseases, Karadeniz Technical University, Faculty of Medicine, Trabzon, Turkey
[23]Department of Pulmonary Diseases, Ankara Atatürk Training and Research Hospital, Ankara, Turkey

Cite this article as: Şenol E, Çilli A, Günen H, *et al*. The role of pneumococcal pneumonia among community-acquired pneumonia in adult turkish population: TurkCap study. *Turk Thorac J.* 2021; 22(4): 339-345.

Abstract

OBJECTIVE: To evaluate the rate of pneumococcal pneumonia (PP) among patients with community-acquired pneumonia (CAP) in Turkey and to investigate and compare features of PP and non-PP CAP patients.

MATERIAL AND METHODS: This multicenter, non-interventional, prospective, observational study included adult CAP patients (age ≥ 18 years). Diagnosis of PP was based on the presence of at least 1 positive laboratory test result for *Streptococcus pneumoniae* (blood culture or sputum culture or urinary antigen test [UAT]) in patients with radiographic findings of pneumonia.

RESULTS: Four hundred sixty-five patients were diagnosed with CAP, of whom 59 (12.7%) had PP. The most common comorbidity was chronic obstructive pulmonary disease (30.1%). The mean age, smoking history, presence of chronic neurological disease, and CURB-65 score were significantly higher in PP patients, when compared to non-PP patients. In PP patients, 84.8% were diagnosed based ony on the UAT. The overall rate of PP patients among CAP was calculated as 22.8% considering the UAT sensitivity ratio of 63% (95% confidence interval: 45-81). The rate of intensive care treatment was higher in PP patients (P = .007). While no PP patients were vaccinated for pneumococcus, 3.8% of the non-PP patients were vaccinated (P = .235). Antibiotic use in the preceding 48 hours was higher in the non-PP group than in the PP group (31.8% vs. 11.1%, P = .002). The CURB-65 score and the rate of patients requiring inpatient treatment according to this score were higher in the PP group.

CONCLUSION: The facts that PP patients were older and required intensive care treatment more frequently as compared to non-PP patients underline the burden of PP.

KEYWORDS: Streptococcus pneumoniae, community-acquired pneumonia, adult
Received: *September 9, 2020* ***Accepted:*** *March 2, 2021*

INTRODUCTION

Streptococcus pneumoniae (pneumococcus) is one of the significant causes of morbidity and mortality worldwide. Pneumococcal infections are more prevalent among children and the elderly, and cause the death of nearly 1 million children aged < 5 years annually.[1] The burden of pneumococcal disease in adults is determined by community-acquired

Corresponding author: Esin Şenol, e-mail: esin.esenol@gmail.com

pneumonia (CAP).[2] The annual incidence rate of CAP has been reported to vary from 1.6 to 11.6 cases per 1000 persons in the general adult population.[3-5] Despite advanced diagnostic techniques, effective antibiotic treatment, and intense cardiopulmonary supportive treatment approaches, CAP remains a common cause of morbidity and mortality.[6] *S. pneumoniae* is a major causative microorganism of CAP.[7] In daily practice, only 20% of CAP cases are microbiologically diagnosed, and this rate increases only to 60% even with the extensive use of expensive diagnostic tests.[2,8,9] Primarily, knowing the regional epidemiological and clinical characteristics of the relevant disease is important to create regional strategies to reduce CAP-related morbidity and mortality. This study aimed to evaluate the rate of pneumococcal pneumonia (PP) among adult patients with CAP in Turkey. Moreover, features of PP and non-PP CAP patients were investigated and compared. We present the following article in accordance with the STROBE reporting checklist.

MATERIAL AND METHODS

This multicenter, non-interventional, prospective, observational study was carried out in 22 centers from 12 regions of Turkey according to the Statistical Office of the European Union (EuroStat) Classification Level 1 (NUTS 1). Adult CAP patients (age ≥ 18 years) who were admitted to the outpatient clinic or emergency room of the relevant centers during a 3-month period (from November 1, 2016 to January 31, 2017) were enrolled into the study. Patients with lung cancer, tuberculosis, and immune deficiency/immune suppression, and patients living in nursing homes for a long time were excluded. The trial was conducted in accordance with the Declaration of Helsinki. The study was approved by the ethics board of Gazi University (No: E.82934) and informed consent was taken from all the patients.

In addition to the patients' demographic information, their vital signs, symptoms, comorbidities, immunization status against pneumonia and influenza, smoking and alcohol consumption, lung radiography findings, information on blood and sputum cultures, results of gram staining performed in a good-quality sputum sample (epithelial cell count of < 10 and polymorphonuclear leukocyte count of > 25 in each lower-magnification objective field [10×]), results of urinary *S. pneumoniae* antigen screening performed by the Alere BinaxNOW®, results of some laboratory tests among routine analyses (leukocyte count, neutrophil ratio, lymphocyte ratio, alanine aminotransferase, aspartate transaminase, gamma-glutamyltransferase, alkaline phosphatase, urea, blood urea nitrogen, C-reactive protein, creatinine, blood gases, and procalcitonin), hospitalization or intensive care stay, and scores of CURB-65 (in case urea measurement was lacking, scores of CRB-65[10]) were recorded.

CAP was defined as the lower respiratory tract infection that occurs in the population during daily life and is characterized by coughing, fever, chilling, fatigue, dyspnea, and pleuritic chest pain, together with infiltrates seen in the chest radiographs.

PP was diagnosed based on the presence of at least 1 positive laboratory test result for *S. pneumoniae* (blood culture or sputum culture or urinary antigen test [UAT]) in patients with radiographic findings of pneumonia. PP patients with positive blood culture for pneumococcus were defined as bacteremic PP.

Statistical Analysis

Data were analyzed using the PASW Statistics for Windows, Version 18.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were expressed as number and percentage for categorical variables and as median, percentile 25 (Q1), and percentile 75 (Q3) for numerical variables. Pairwise comparison between categorical variables was performed using the chi-square test, and when the condition for chi-square was not met, Fisher's exact test was used. The level of Type 1 error below 5% was considered statistically significant.

RESULTS

Over the study period, the number of patients screened for the study in 22 study centers was 69614, and the number of patients treated as inpatients was 6622. A total of 465 patients (0.61%) were diagnosed with CAP in accordance with the above mentioned definition (Figure 1). Of the patients, 61.5% were male and the median age was 69 years (range, 54-78 years). Chronic obstructive pulmonary disease (COPD) was the most common comorbidity in 30.1% (n = 140) of the patients diagnosed with CAP. Of the patients, 71.6% were treated as inpatients. The general characteristics of the CAP patients are summarized in Table 1.

Fifty-nine (12.7%) of the CAP patients were diagnosed with PP. Among these patients, only UAT test was positive in 50 patients, only blood culture was positive in 2 patients, only sputum culture was positive in 2 patients, sputum culture + UAT test were positive in 3 patients, blood culture + UAT test were positive in 1 patient, and blood culture + sputum culture + UAT test were positive in 1 patient.

One of the patients was not assigned to either group and was excluded from the analysis as none of the results (blood culture, sputum culture, or pneumococcal UAT) was available. Comparison between the characteristics of PP (n = 59) and non-PP (n = 405) patients is demonstrated in Table 2. Patients with PP were older, had a longer history of smoking, and had higher rates of chronic neurological comorbidity. The

MAIN POINTS

- This first nationwide study revealed the role of pneumococcal pneumonia (PP) in the etiology of community acquired pneumonia (CAP) in adults.
- Among CAP patients, 12.7% had PP, of whom 76.3% were inpatient.
- The facts that PP patients were older and required intensive care treatment more frequently as compared to the non-PP patients underline the PP burden.
- Very low vaccination rates for pneumococcus and influenza and high rates of empirical antibiotic use among CAP patients reveals the need for better understanding of CAP epidemiology.

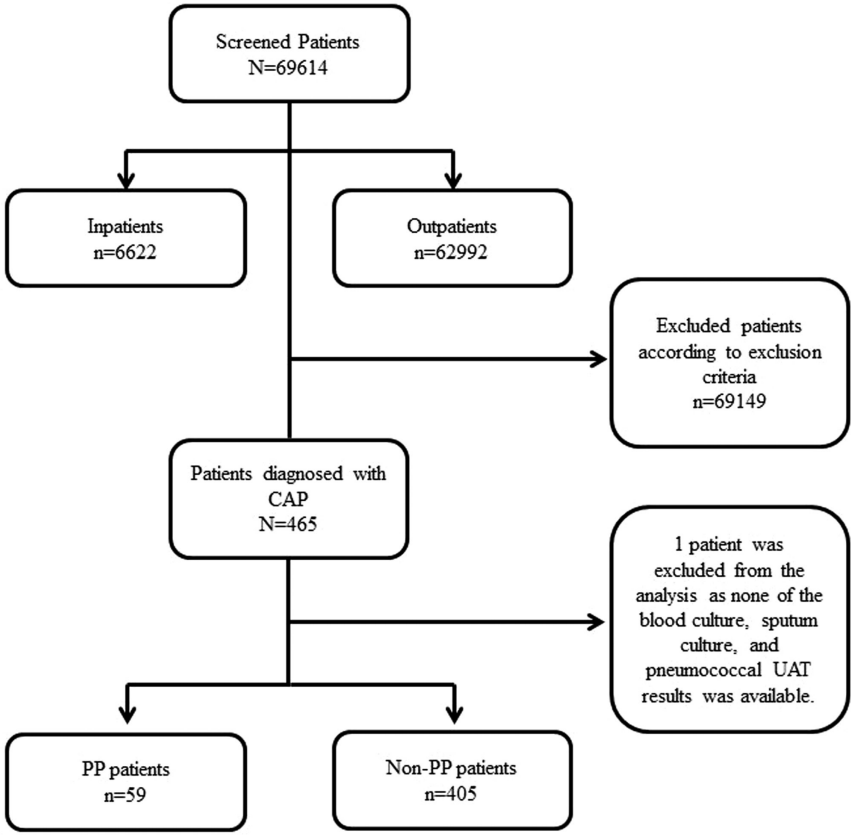

Figure 1. Study flow diagram. CAP, community-acquired pneumonia; PP, pneumococcal pneumonia; UAT, urinary antigen test.

diagnosis was performed based only on positive UAT in 50 (84.8%) of the 59 PP patients. Sensitivity of the Alere BinaxNOW® *S. pneumoniae* Antigen Card was reported as 63% (95% CI: 45-81).[11] Considering this, the ratio of PP patients among CAP patients was estimated to be 22.8%.

The signs and symptoms and hospitalization statuses of the PP and non-PP CAP patients are summarized in Table 3. The rate of intensive care treatment was significantly higher in the PP group compared with that in the non-PP group (24.4% vs. 10.2%, $P = .007$).

While none of the patients had been vaccinated for pneumococcus in the PP group, 3.8% of the patients in the non-PP group were vaccinated ($P = .235$). The rates of vaccination for influenza in the PP and non-PP groups were 5.2% and 9.2%, respectively ($P = .304$). Antibiotic use in the preceding 48 hours was higher in the non-PP patients as compared with the PP patients (31.8% vs. 11.1%, $P = .002$).

The CURB-65 score and the rate of patients requiring inpatient treatment according to this score were higher in the PP group (Table 4).

DISCUSSION

In the present study, the general characteristics of 465 patients diagnosed with CAP were evaluated. Of the patients, 61.5% were male, and the median age was 69 years. It has been reported that the incidence of CAP increases with age.[12] In the present study, the prevalence of patients aged ≥ 65 years was 60%. The prevalence of inpatient treatment among CAP patients has been reported as between 20 and 45%[13-15] and nearly 10-20% of these patients require intensive care treatment.[12,16] In the present study, 71.6% of CAP patients received inpatient treatment and intensive care treatment was required in 12.1% of these patients.

Cardiovascular diseases, COPD, and diabetes were reported to be the most common comorbidities in CAP patients.[14,17-19] COPD has been reported in 19-43% of the CAP patients.[14,17-19] In the present study, COPD was the most common comorbidity determined in 30.1% of the CAP patients.

Distribution of the microorganisms playing a role in the etiology of CAP shows variation among studies. Many factors including geographic region, patient characteristics (advanced age, comorbidity, risk-prone groups, etc.), and seasonal features may have a role in this distribution.[20,21] In addition, there may be many different factors (antibiotic use, vaccination, etc.) affecting CAP, and the rates may change over time. Therefore, it is important to determine the factors promptly. The present study reported the latest CAP factors in the country and the rate of PP among these factors. In the studies, *S. pneumoniae* was isolated as the agent microorganism in 5-30% of CAP patients depending on the use of traditional or molecular techniques.[8,9,12,17,18,22-25] In the present study, *S. pneumoniae* was determined as the pathogenic agent in 12.7% of the CAP patients based on the positivity in at least 1 microbiological test.

In general, CAP patients are treated with empirical antimicrobial therapy. Early diagnosis of the agent would favorably influence the prognosis by leading to appropriate antibiotic use.[20] Since conventional tests like culture take several days, there is a need for rapid tests. For this reason, the use

Table 1. General Characteristics of the CAP Patients

	N	Values
Gender, *n* (%)	465	
Female		179 (38.5)
Male		286 (61.5)
Age, year, median (Q1-Q3)		69 (54-78)
Current smoker, *n* (%)	451	59 (13.1)
Regular alcohol consumer, *n* (%)	454	9 (2.0)
The most common comorbidity—COPD, *n* (%)	465	140 (30.1)
The most common symptom—cough, *n* (%)	465	386 (83.0)
Lung radiography findings, *n* (%)	465	
Unilateral		297 (63.9)
Bilateral		141 (30.3)
Unilober		176 (37.8)
Multilober		115 (24.7)
Pleural effusion		46 (9.9)
Microbiological results, *n* (%)	162	
Blood culture-growth (+)		
Streptococcus pneumoniae		4 (2.5)
Gram (–) enteric bacteria		3 (1.9)
Other		11 (6.8)
Blood culture-growth (–)		144 (88.9)
Sputum culture-growth (+)		
Streptococcus pneumoniae		6 (3.7)
Gram (–) enteric bacteria		4 (2.5)
Staphylococcus aureus		1 (0.6)
Moraxella catarrhalis		1 (0.6)
Gram (–) enteric bacteria + non-fermenting gram (–) bacilli		1 (0.6)
Other		22 (13.6)
Sputum culture-growth (–)		127 (78.4)
Positive pneumococcal UAT	464	55 (11.9)
Positive *Legionella pneumophila* UAT	88	7 (8.0)
Inpatient treatment, *n* (%)	465	333 (71.6)
Intensive care treatment, *n* (%)	330	40 (12.1)
Vaccination for pneumococcus, *n* (%)	458	15 (3.3)
Vaccination for influenza, *n* (%)	459	40 (8.7)
CURB-65, median (Q1-Q3)	432	2 (1-2)

Q1, 25th percentile; Q3, 75th percentile.
COPD, chronic obstructive pulmonary disease; UAT, urinary antigen test.

of pneumococcal UAT has gradually become widespread and has been found beneficial in the etiological diagnosis of lower respiratory tract infections.[26,27] In the present study, 84.8% of the PP patients were diagnosed based on UAT positivity alone. The overall rate of PP patients among CAP patients was calculated as 22.8%, considering the UAT sensitivity ratio of 63% (95% CI: 45-81).

In the present study, comparison between the PP and non-PP CAP patients revealed that the PP patients were older, had a longer history of smoking, and a higher rate of chronic neurological comorbidity. There was no difference between PP and non-PP CAP patients in terms of presenting signs and symptoms. Although it did not reach statistical significance, the rate of inpatient treatment was found higher in the PP patients compared with the non-PP patients (76.3% vs. 70.9%). The rate of intensive care treatment was also higher in the PP patients than in the non-PP patients (24.4% vs. 10.2%, $P = .007$).

In the present study, none of the patients had taken the pneumococcal vaccination in the PP group, whereas 3.8%

Table 2. General Characteristics of PP and Non-PP CAP Patients

	N	PP	*N*	Non-PP	*P*
Gender, *n* (%)	59		405		
Female		16 (27.1)		163 (40.2)	.053
Male		43 (72.9)		242 (59.8)	
Age, year, median (Q1-Q3)	59	73 (60-83)	404	68 (53-78)	.027
Smoking, n (%)	56		394		
Never smoked		34 (60.7)		213 (54.1)	.182
Ex-smoker		19 (33.9)		125 (31.7)	
Current smoker		3 (5.4)		56 (14.2)	
Duration of smoking, year, median (Q1-Q3)	16	38 (30-43)	115	30 (20-40)	.041
Alcohol consumption, n (%)	54		399		
Never		50 (92.6)		355 (89.0)	.499
Social drinker		4 (7.4)		35 (8.8)	
Regular drinker		0 (0.0)		9 (2.3)	
Comorbidity, n (%)	59		405		
COPD		13 (22.0)		126 (31.1)	.155
Diabetes		7 (11.9)		87 (21.5)	.086
Coronary artery disease		9 (15.3)		71 (17.5)	.665
Congestive heart failure		7 (11.9)		67 (16.5)	.359
Chronic neurological disorder		13 (22.0)		29 (7.2)	<.001
Renal failure		3 (5.1)		26 (6.4)	1.000
Malignancy (except Lung Ca)		0 (0.0)		12 (3.0)	.378
Chronic liver disease		1 (1.7)		6 (1.5)	1.000
Mild immune deficiency		1 (1.7)		0 (0.0)	-
Other		18 (30.5)		159 (39.3)	.196

Q1, 25th percentile; Q3, 75th percentile.
COPD, chronic obstructive pulmonary disease; PP, pneumococcal pneumonia.

of the patients in the non-PP group had been vaccinated. Regarding the rate of vaccination for influenza, it was found to be 5.2% and 9.2% in the PP and non-PP groups, respectively. Despite limited data about the rate of adult vaccination, the limited number of studies has revealed very low vaccination rates even in the high-risk groups. For example, the rates of vaccination for pneumococcus and influenza have been reported to be 0.1% and 9.1% in diabetic patients, respectively, and 10-15% and 14.9% in COPD patients,[28] In a multicenter study from Turkey, the rates of vaccination for pneumococcus and influenza were 9.2% and 16.1%, respectively, in the patients hospitalized for CAP. It has been indicated that patients with the comorbidity of COPD have the highest awareness.[29] The beneficial effect of vaccination in protecting against pneumococcal infections is well-known.[30] Considering the results of the present study, there is an obvious need for studies aimed at increasing the rate of vaccination and prioritizing the patients at highest risk, like patients with COPD, in Turkey.

CURB-65 is one of the most commonly used scoring systems to determine the disease severity in CAP patients.[20] The CURB-65 score is used to decide whether CAP patients need to be treated as inpatients. Nevertheless, inconsistency has been reported between scoring and physician's judgment in clinical practice, and extra-hospitalization is in question when the decision is made based on the physicians' judgment rather than scoring.[31,32] Correspondingly, in the present study, the rate of patients requiring inpatient treatment was 49.8% according to the CURB-65 score, whereas it was 71.6% according to the physician's judgment. The CURB-65 score and the rate of patients requiring inpatient treatment were higher in the PP group.

In the present study had several limitations. The use of antibiotics in the preceding 48 hours was not considered an inclusion criterion since it is known that UAT is not influenced by antibiotic use. This may explain the low rates of *S. pneumoniae* as the pathogenic agent, except for the rates obtained by UAT, and can be considered as one of the limitations of the study. We mentioned the sensitivity of UAT for PP as 63%; considering this low sensitivity of UAT as well as the low rate of bacteriological diagnosis, some PP patients might have been evaluated as non-PP patients. Moreover, the role of atypical pathogens and viral agents in CAP was not evaluated. Leukocyte count and C-reactive protein were not evaluated either. This study also lacked mortality data; therefore, the prognostic importance of PP could not be evaluated, although the ratio of intensive care stay was higher in the PP group.

Table 3. Signs and Symptoms and Hospitalization Status of PP and Non-PP CAP Patients

	N	PP	*N*	Non-PP	*P*
Symptoms, *n* (%)	59		405		
Newly developed or worsened cough		49 (83.1)		336 (83.0)	.987
Dyspnea		41 (69.5)		298 (73.6)	.508
Body temperature >38°C		26 (44.1)		181 (44.7)	.928
Fine rales and bronchial breathing		23 (39.0)		169 (41.7)	.689
Pleuritic chest pain		20 (33.9)		157 (38.8)	.472
Tachypnea		25 (42.4)		142 (35.1)	.274
Vital sign, median (Q1-Q3)					
Body temperature (°C)	56	36.8 (36.5-38)	405	36.9 (36.6-37.8)	.470
Pulse rate (beat/min)	57	89 (78-100)	403	88 (80-97)	.715
Respiratory rate (breath/min)	56	22 (20-24)	403	20 (18-24)	.222
Systolic blood pressure (mmHg)	58	115 (110-130)	404	120 (110-130)	.128
Diastolic blood pressure (mmHg)	58	70 (60-80)	404	70 (65-80)	.575
Type of treatment, *n* (%)	59		405		
Outpatient		14 (23.7)		118 (29.1)	.390
Inpatient		45 (76.3)		287 (70.9)	
Department, *n* (%)	45		284		
Clinic		34 (75.6)		255 (89.8)	.007
Intensive care		11 (24.4)		29 (10.2)	

Q1, 25th percentile; Q3, 75th percentile.
PP, pneumococcal pneumonia.

Table 4. Severity Score in PP and Non-PP CAP Patients

	N	PP	*N*	Non-PP	*P*
CURB-65 score, median (Q1-Q3)	58	2 (1-3)	373	1 (1-2)	.002
CRB-65 score, median (Q1-Q3)	1	0 (0-0)	32	0 (0-1)	-
According to CURB-65 or CRB-65 score	59		405		
Need for outpatient treatment, *n* (%)		19 (32.2)		214 (52.8)	.003
Need for inpatient treatment, *n* (%)		40 (67.8)		191 (47.2)	

Q1, 25th percentile; Q3, 75th percentile.
PP, pneumococcal pneumonia.

In the present study, 12.7% of the CAP patients were PP patients. The fact that the PP patients were older and required intensive care treatment more frequently as compared with the non-PP patients underlines the burden of PP. Very low vaccination rates for pneumococcus and influenza among CAP patients suggest the necessity of studies aimedg at increasing both the awareness and the vaccination rates.

Ethics Committee Approval: This study was approved by the Ethics committee of Gazi University (Approval No: E.82934)

Informed Consent: Written informed consent was obtained from the patients who agreed to take part in the study.

Peer Review: Externally peer-reviewed.

Author Contributions: Supervision – E.S., A.C., H.G., A.S., R.D., A.O., A.F.T., Y.Y., R.G., A.O., B.M., N.K., N.S., N.B., D.Y., S.E., M.P., S.E.G., O.K., A.S., O.K., Ç.Ç., A.S.K., T.T., H.A., H.K., I.K., F.A., C.H.; Design – E.S., A.C., H.G., A.S., R.D., A.O., A.F.T., Y.Y., R.G., A.O., B.M., N.K., N.S., N.B., D.Y., S.E., M.P., S.E.G., O.K., A.S., O.K., Ç.Ç., A.S.K., T.T., H.A., H.K., I.K., F.A., C.H.; Concept – E.S., A.C., H.G., A.S., R.D., A.O., A.F.T., Y.Y., R.G., A.O., B.M., N.K., N.S., N.B., D.Y., S.E., M.P., S.E.G., O.K., A.S., O.K., Ç.Ç., A.S.K., T.T., H.A., H.K., I.K., F.A., C.H.; Resources – E.S., A.C.; Materials – E.S., A.C.; Data Collection and/or Processing – E.S., A.C., H.G., A.S., R.D., A.O., A.F.T., Y.Y., R.G., A.O., B.M., N.K., N.S., N.B., D.Y., S.E., M.P., S.E.G., O.K., A.S., O.K., Ç.Ç., A.S.K., T.T., H.A., H.K., I.K., F.A., C.H.; Analysis and/or Interpretation – E.S., A.C.; Literature Search – E.S., A.C.; Writing Manuscript – E.S., A.C., H.G., A.S., R.D., A.O., A.F.T., Y.Y., R.G., A.O., B.M., N.K., N.S., N.B., D.Y., S.E., M.P., S.E.G., O.K., A.S., O.K., Ç.Ç., A.S.K., T.T., H.A., H.K., I.K., F.A., C.H.; Critical Review – E.S., A.C.

Conflict of Interest: Esin Şenol, Aykut Çilli, Ayhan Özhasenekler, Birsen Mutlu, Nurcan Baykam, Selami Ekin, Mehmet Polatlı, Şebnem Eren Gök, Ömer Karaşahin, Turhan Togan, Hüseyin Arpağ, İftihar Köksal, and Firdevs Aksoy have received a travel grant and an

honorarium from Pfizer Pharmaceuticals; Hakan Günen, Rahmet Güner, and Nurdan Köktürk have received an honorarium from Pfizer Pharmaceuticals; YeşimYıldız has received a travel grant from Pfizer Pharmaceuticals; Abdullah Sayıner has received honoraria for giving lectures in Pfizer-sponsored meetings and has served on the local advisory board of Pfizer; Çağlar Çuhadaroğlu has received an honorarium from Pfizer Pharmaceuticals and a travel grant from Sanofi Aventis. The other authors have no conflicts of interest to declare.

Financial Disclosure: This work was supported by Pfizer Pharmaceuticals, Turkey.

REFERENCES

1. Henriques-Normark B, Tuomanen EI. The pneumococcus: epidemiology, microbiology, and pathogenesis. *Cold Spring Harb Perspect Med*. 2013;3:a010215-a010215. [CrossRef]
2. Drijkoningen JJ, Rohde GG. Pneumococcal infection in adults: Burden of disease. *Clin Microbiol Infect*. 2014;20:45-51. [CrossRef]
3. Almirall J, Bolíbar I, Vidal J et al. Epidemiology of community-acquired pneumonia in adults: a population-based study. *Eur Respir J*. 2000;15:757-763. [CrossRef]
4. Kolditz M, Tesch F, Mocke L et al. Burden and risk factors of ambulatory or hospitalized CAP: a population based cohort study. *Respir Med*. 2016;121:32-38. [CrossRef]
5. Blasi F, Akova M, Bonanni P et al. Community-acquired pneumonia in adults: highlighting missed opportunities for vaccination. *Eur J Intern Med*. 2017;37(8118):13-18. [CrossRef]
6. Wunderink RG, Waterer G. Advances in the causes and management of community acquired pneumonia in adults. *BMJ*. 2017;358:j2471. [CrossRef]
7. Steel HC, Cockeran R, Anderson R, Feldman C. Overview of community-acquired pneumonia and the role of inflammatory mechanisms in the immunopathogenesis of severe pneumococcal disease. *Mediators Inflamm*. 2013;2013:490346. [CrossRef]
8. Holter JC, Müller F, Bjørang O et al. Etiology of community-acquired pneumonia and diagnostic yields of microbiological methods: a 3-year prospective study in norway. *BMC Infect Dis*. 2015;15(11):64. [CrossRef]
9. Ieven M, Coenen S, Loens K et al. Aetiology of lower respiratory tract infection in adults in primary care: a prospective study in 11 european countries. *Clin Microbiol Infect*. 2018;24:1158-1163. [CrossRef]
10. Lim WS, van der Eerden MM, Laing R et al. Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study. *Thorax*. 2003;58:377-382. [CrossRef]
11. Saukkoriipi A, Pascal T, Palmu AA. Evaluation of the BinaxNOW® Streptococcus pneumoniae antigen test on fresh, frozen and concentrated urine samples in elderly patients with and without community-acquired pneumonia. *J Microbiol Methods*. 2016;121(5):24-26. [CrossRef]
12. Jain S, Self WH, Wunderink RG et al. Community-acquired pneumonia requiring hospitalization among U.S. adults. *N Engl J Med*. 2015;373:415-427. [CrossRef]
13. Broulette J, Yu H, Pyenson B, Iwasaki K, Sato R. The incidence rate and economic burden of community-acquired pneumonia in a working-age population. *Am Health Drug Benefits*. 2013;6:494-503. [CrossRef]
14. Bertsias A, Tsiligianni IG, Duijker G et al. Studying the burden of community-acquired pneumonia in adults aged ≥50 years in primary health care: an observational study in rural Crete, Greece. *NPJ Prim Care Respir Med*. 2014;24(11):14017. [CrossRef]
15. Kabundji DM, Musekiwa A, Mukansi M, Feldman C. Determining need for hospitalisation: evaluation of the utility of the CRB-65 score in patients with community-acquired pneumonia presenting to an emergency department. *S Afr Med J*. 2014;104:769-772. [CrossRef]
16. Kaysin A, Viera AJ. Community-acquired pneumonia in adults: diagnosis and management. *Am Fam Phys*. 2016;94:698-706. [CrossRef]
17. Parrott G, Nebeya D, Kinjo T et al. Etiological analysis and epidemiological comparison among adult CAP and NHCAP patients in Okinawa, Japan. *J Infect Chemother*. 2017;23:452-458. [CrossRef]
18. Köksal I, Ozlü T, Bayraktar O et al. Etiological agents of community-acquired pneumonia in adult patients in turkey; a multicentric, cross-sectional study. *Tuberk Toraks*. 2010;58:119-127.
19. Spoorenberg SM, Bos WJ, Heijligenberg R et al. Microbial aetiology, outcomes, and costs of hospitalisation for community-acquired pneumonia; an observational analysis. *BMC Infect Dis*. 2014;14:335. [CrossRef]
20. Remington LT, Sligl WI. Community-acquired pneumonia. *Curr Opin Pulm Med*. 2014;20:215-224. [CrossRef]
21. Sahuquillo-Arce JM, Menéndez R, Méndez R et al. Age-related risk factors for bacterial aetiology in community-acquired pneumonia. *Respirology*. 2016;21:1472-1479. [CrossRef]
22. Harat R, Alexander R, Gray S et al. Prospective, population-based surveillance of the burden of streptococcus pneumoniae in community-acquired pneumonia in older adults, chrzanów county, poland, 2010-2012. *Pneumonol Alergol Pol*. 2016;84:95-103. [CrossRef]
23. Cilloniz C, Ewig S, Gabarrus A et al. Seasonality of pathogens causing community-acquired pneumonia. *Respirology*. 2017;22:778-785. [CrossRef]
24. Naderi H, Sheybani F, Sarvghad M, Meshkat Z, Jabbari Nooghabi M. Etiological diagnosis of community-acquired pneumonia in adult patients: a prospective hospital-based study in Mashhad, Iran. *Jundishapur J Microbiol*. 2015;8:e22780. [CrossRef]
25. Gelfer G, Leggett J, Myers J, Wang L, Gilbert DN. The clinical impact of the detection of potential etiologic pathogens of community-acquired pneumonia. *Diagn Microbiol Infect Dis*. 2015;83:400-406. [CrossRef]
26. Camou F, Issa N, Bessede É, Mourissoux G, Guisset O. Usefulness of pneumococcal antigen urinary testing in the intensive care unit? *Med Mal Infect*. 2015;45:318-323. [CrossRef]
27. Choi MJ, Song JY, Cheong HJ et al. Clinical usefulness of pneumococcal urinary antigen test, stratified by disease severity and serotypes. *J Infect Chemother*. 2015;21:672-679. [CrossRef]
28. Alici DE, Sayiner A, Unal S. Barriers to adult immunization and solutions: personalized approaches. *Hum Vaccin Immunother*. 2017;13:213-215. [CrossRef]
29. Demirdogen Cetinoglu E, Uzaslan E, Sayıner A et al. Pneumococcal and influenza vaccination status of hospitalized adults with community acquired pneumonia and the effects of vaccination on clinical presentation. *Hum Vaccin Immunother*. 2017;13:2072-2077. [CrossRef]
30. van Werkhoven CH, Bonten MJ. The community-acquired pneumonia immunization trial in adults (CAPiTA): what is the future of pneumococcal conjugate vaccination in elderly? *Future Microbiol*. 2015;10:1405-1413. [CrossRef]
31. Ullah S, Khan J, Khan A, Hashemy I. Assessing decision of inpatient or outpatient care in community acquired pneumonia: APT care study. *J Pak Med Assoc*. 2017;67:380-385.
32. Guo Q, Li HY, Zhou YP et al. Compliance with the CURB-65 score and the consequences of non-implementation. *Int J Tuberc Lung Dis*. 2011;15:1697-1702. [CrossRef]