

# Infectious Etiology of Hospitalized Community-Acquired Pneumonia Patients in Turkey

## Türkiye’de Toplum Kökenli Pnömoni Tanısıyla Hospitalize Edilen Hastalarda Etkenler

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### SUMMARY

*This paper aims to evaluate the causative agents in patients hospitalized due to community-acquired pneumonia in Turkey. Fourteen local studies are assessed and pneumococci are the main etiological agents followed by enteric gram-negative bacilli, streptococci other than pneumococci, Staphylococcus aureus and Haemophilus influenzae. On the other hand, Mycoplasma species are the leading etiological agents preceding Chlamydia and Legionella in atypical pneumonia that comprise 29% of community-acquired pneumonia in Turkey.*

**Key Words:** Community-acquired infections, Pneumonia, Etiology, Turkey

### ÖZET

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*Bu makale Türkiye’de toplum kökenli pnömoni nedeni ile hastanelere yatırılan hastalarda etkenleri irdelemeyi amaçlamaktadır. On dört bölgesel çalışma irdelenmiştir. Pnömonokoklar birincil etkindir ve ardından enterik gram-negatif bakteriler, pnömokok dışı streptokoklar, Staphylococcus aureus ve Haemophilus influenzae gelmektedir. Diğer yandan, atipik pnömonilerde en sık Mycoplasma türleri, ardından Chlamydia ve Legionella grubu bakteriler görülmektedir. Atipik pnömoniler Türkiye’de tüm pnömonilerin %29’unu oluşturmaktadır.*

**Anahtar Kelimeler:** Toplum kökenli enfeksiyonlar, Pnömoni, Etiyoloji, Türkiye

## COMMUNITY-ACQUIRED PNEUMONIA in TURKEY

According to Turkish Ministry of Health and State Statistical Institute data, pneumonia is an important problem in Turkey<sup>[1]</sup>. In the final report, which declared the results of "Disease Intensity and Cost Effectivity Project" in 2004, pneumonia was the 15<sup>th</sup> disease detected in the community in the last 2 months. In this study, lower respiratory tract infections in adults were reported to be the fifth disease in terms of fatality rates. Moreover, pneumonia was the fifth disease according to disability adjusted life year analysis in that report<sup>[2]</sup>. On the other hand, lower respiratory tract infections comprised 2.8% of all outpatient visits in a local study in the northeast part of the country. In 2004, approximately 112.000 bacterial pneumonia cases were hospitalized throughout the country with the resultant fatality of 1.5%. In addition, 5500 viral pneumonias were treated in the hospitals and the fatality rate was 1.3%<sup>[3]</sup>. Consequently, the microbial epidemiology of bacterial pneumonias, which comprise most of the hospitalizations due to lung infections and an important portion of outpatient visits, is very crucial in Turkey.

Turkey is a large country with total population of 74 million and the gross national income per capita is around 9000 American Dollars. Life expectancy is 71 for males and 75 for females, although healthy life expectancy is 61 and 63 years respectively. Mortality rate under five per 1000 live births is 26. Total expenditure on health as a percentage of gross domestic products is 5.7%<sup>[4]</sup>. According to these parameters Turkey seems to be a developing and a reorganizing country. In this article infectious agents in community-acquired pneumonia (CAP) are assessed on a regional basis in Turkey to enlighten clinical approaches in these cases.

### ETIOLOGY of COMMUNITY-ACQUIRED PNEUMONIA

The publications related with the pathogens of CAP in both national (Ulakbim and Pleksus) and international (Medline) databases along with the presentations either in clinical microbiology or infectious diseases congress books were searched and analysed. The studies published since 1997 were included in this review.

Publications including blood, sputum and bronchoalveolar lavage fluid culture results and serological analysis for atypical pathogens in patients with clinical diagnosis of pneumonia were included in this study.

The laboratory based CAP studies in Turkey generally did not focus on all respiratory pathogens; rather they used either the culture methods or the serological tests depending on the availability of the test methods at that particular time.

The local studies unfortunately did not combine clinical and microbiological data. So only the microbiological results of the respiratory pathogens were reported. The clinical features of the patients (eg. hospitalization in intensive care unit etc.) were not reported in accordance with the guidelines used in developed countries.

There are twelve studies reporting culture results of CAP patients in Turkey and for epidemiological purposes eight studies reported the pathogen distribution of atypical microorganisms<sup>[5-18]</sup>. The distribution of pathogens in CAP patients in Turkey and the multiple atypical etiologies are presented in Table 1 and Table 2 respectively.

The agents of CAP were obtained by bronchoscopic methods in 22 patients. In two publications assessing both typical and atypical pathogens, additional atypical microorganisms were reported in eight of 132 patients (seven *Mycoplasma pneumoniae*, one *Chlamydia pneumoniae*)<sup>[7,10]</sup>. Similarly in an article pneumococci was the infecting agent with EGNB in two cases while in two other patients *Pseudomonas aeruginosa* was the concordant pathogen<sup>[7]</sup>.

### CLINICAL APPROACH to COMMUNITY- ACQUIRED PNEUMONIA

Developing countries are not homogeneous in their clinical approach to CAP. Variety in antibiotic use habits, different antibiotic resistance patterns, defective hospital infrastructures and poor patient access to hospitals when necessary during outpatient therapy lead to different management strategies in CAP. Combined with the absence of compulsory national algorithms on the decision of hospitalization, the clinicians attempt to manage patients according to their individual approach and in Turkey, the gene-

**Table 1. Cumulative distribution of pathogens in CAP patients in Turkey**

	Patients	Culture positive (%)	References	Pathogens	Percentage
• Pyogenic bacteria	806	344 (43%)	[5-16]	<i>Streptococcus pneumoniae</i>	45%
				EGNB	15%
				Streptococci*	10%
				<i>Staphylococcus aureus</i>	9%
				<i>Haemophilus influenzae</i>	7%
				<i>Pseudomonas aeruginosa</i>	6%
				<i>Neisseria</i> spp.	4%
				<i>Moraxella catarrhalis</i>	2%
• Atypical pathogens	566	Serology (+) 200 seropositives in 166 CAP patients	[5-10,17,18]	<i>Mycoplasma pneumoniae</i>	50%
				<i>Chlamydia pneumoniae</i>	35.5%
				<i>Legionella pneumophila</i>	10%
				<i>Coxiella burnetti</i>	4.5%

\* Nonpneumococcal.

CAP: Community-acquired pneumonia, EGNB: Enteric gram-negative bacilli.

**Table 2. Multiple infections with atypical agents<sup>[5-10,17,18]</sup>**

	<i>Mycoplasma pneumoniae</i>	<i>Chlamydia pneumoniae</i>	<i>Legionella pneumophila</i>	<i>Coxiella burnetti</i>
• <i>Mycoplasma pneumoniae</i>		20		1
• <i>Chlamydia pneumoniae</i>			3	2
• <i>Coxiella burnetti</i>	4*			
• TOTAL		64 seropositives in 30 cases		

\* Triple etiology.

ral approach among clinicians is to hospitalize all CAP patients. Major reason underlying this approach may be the disbelief on compliance of the patient to the medication prescribed. Similarly, the decision of hospitalization in intensive care unit (ICU) is generally made subjectively by clinicians according to their personal experience rather than adhering to objective algorithms. Although, this situation may present flexibility to the physicians, lack of standardization is the inevitable result. An algorithm, similar to the American guideline, is published in 2002 as a consensus paper by Turkish Thorax Society (TTS)<sup>[19]</sup>. Recently TTS has prepared a new and updated CAP guideline with the participation of pulmonologists, microbiologists, internal medicine and infectious diseases specialists. This new consensus paper that considers the regional data much more than the previous one is about to be published in 2009.

The major CAP guidelines of the developed countries for the treatment of CAP generally differentiate between outpatients, inpatients, and patients hospitalized in intensive care units. The pathogen distribution and the diagnostic approaches are disclosed according to these categories in these guidelines<sup>[20-22]</sup>. The current American guideline recommends the use of diagnostic bronchoscopy for culture in ICU patients<sup>[20]</sup>. Twenty-two patients that we assessed in this review were inspected by bronchoscopy to obtain culture samples and the clinical features of these patients were obscure in these articles. Consequently, the microbiological data verified from local publications which assess hospitalized patients in Turkey do not differentiate between the results, pathogen distribution and clinical findings among the a forementioned three categories.

Antibiotic resistance of the respiratory pathogens has been increasing steadily in Turkey. Counter availability and self use of antibiotics are possible but in that case patients should pay themselves. Given the fact that the social security covers nearly all of the citizens, people generally prefer to apply to a medical institution to get a prescription. This fact is in favor of limiting antibiotic resistance. But on the other hand, the excessive use of antibiotics more than a half century in Turkey resulted in an increasing pattern of antibiotic inefficacy. For example, the cumulative penicillin resistance of *Streptococcus pneumoniae* isolates the most prevalent microorganism in CAP in Turkey, has risen from 10% in the late 1980s to 35% today. However, penicillin resistance of less than 4 µg/mL does not correlate with therapeutic failures in CAP; thus 35% of penicillin resistance does not have much clinical significance in the management of pneumococcal CAP in Turkey. The decrease in susceptibility is of particular concern for other antibiotics used in CAP and strict surveillance is necessary to delineate suitable therapeutic modalities on a regional basis<sup>[19,23-25]</sup>. Since CAP is historically known as “the most fatal form of acute infectious diseases” stated by Sir William Osler, trailing the share of pathogens in pneumonia is of utmost importance. Thus, surveillance has two arms, one is the distribution of the causative agents in a specific localization and the other is the detection of antibiotic susceptibilities.

Pneumococci are the main etiological agents in CAP requiring hospitalization in Turkey. Moreover, EGNB, *P. aeruginosa* and *Staphylococcus aureus* are not infrequent in hospitalized CAP in our country and these microorganisms cause infections difficult to treat in which caution is indicated for either increased antibiotic resistance or particular virulence characteristics<sup>[26,27]</sup>. For this reason the use of culture methods in critically ill patients is imperative. On the other hand, *Mycoplasma* species are the leading etiological agents followed by *Chlamydia* in atypical pneumonias that comprise nearly one third of CAP in Turkey. Another infection that is hard to control is Legionellosis which is responsible from one tenth of all atypical CAP cases. The mortality of community-acquired Legionnaires' disease is up to 30% if untreated and the mortality for nosocomial Legionnaires' disease can be as high as 50% given the underlying

illness of the patient<sup>[28]</sup>. There are no clinical symptoms, findings, or chest radiograph appearances that reliably distinguish atypical pneumonia from a pyogenic CAP. An additional difficulty in making an etiologic diagnosis in atypical pneumonia is that the pathogens are often difficult to culture, leading to reliance upon serologic methods<sup>[28-30]</sup>. The use of microbiological diagnostic tests for atypical pathogens is not generally recommended in routine practice, the only exception of which is legionellosis. Legionella testing is recommended in ICU patients, active alcohol abusers and those with pleural effusion<sup>[20]</sup>. Thus, the clinician should consider legionellosis and pyogenic bacteria in serious patients and should not overlook these fatal infections.

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