Jundishapur J Microbiol. 2015 August; 8(8): e22780. DOI: 10.5812/jjm.22780

Published online 2015 August 29. **Research Article**

Etiological Diagnosis of Community-Acquired Pneumonia in Adult Patients: A Prospective Hospital-Based Study in Mashhad, Iran

Hamidreza Naderi [1]; Fereshte Sheybani [1,*]; Mohammadreza Sarvghad [1]; Zahra Meshkat [2]; Mehdi Jabbari Nooghabi [3]

[1]Department of Infectious Diseases, Imam Reza Teaching Hospital, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, IR Iran
[2]Department of Clinical Microbiology and Virology, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, IR Iran
[3]Department of Statistics, Faculty of Mathematics, Ferdowsi University, Mashhad, IR Iran

*Corresponding author: Fereshte Sheybani, Department of Infectious Diseases, Imam Reza Teaching Hospital, Faculty of Medicine, Mashhad University of Medical Sciences, Mashhad, IR Iran. Tel: +98-9151254062, Fax: +98-5138407742, E-mail: fereshtesheybani@gmail.com; sheybanif@mums.ac.ir

Received: August 14, 2014; **Revised:** October 22, 2014; **Accepted:** November 10, 2014

Background: Pneumonia is the third most common cause of death in the world, and mortality is highest for patients who require hospitalization.

Objectives: This prospective observational study is an etiological survey of community-acquired pneumonia (CAP) over a 12-month period in the Iranian city of Mashhad. To our knowledge, this is one of the first prospective hospital-based studies to comprehensively evaluate the epidemiological, demographical, clinical, and prognostic factors of patients with CAP in Iran.

Patients and Methods: We studied all adult patients (aged ≥16 years) with CAP admitted to Imam Reza Hospital, Mashhad, Iran, between February 2013 and January 2014. The etiological diagnosis of CAP was made through conventional culturing and staining of respiratory secretions (i.e. sputum and pleural fluid), standard BACTEC™ Plus Aerobic/F bottles for blood cultures, and the immunochromatographic assays BinaxNOW® *Streptococcus pneumoniae* antigen and BinaxNOW® *Legionella pneumophila* antigen for the detection of *S. pneumoniae* antigen and *L. pneumophila* serogroup 1 antigen, respectively.

Results: Among 120 patients with CAP, the most common etiology was *S. pneumoniae* (24.4%), followed by *Mycobacterium tuberculosis* (17.5%), *S. aureus* (6.7%), polymicrobial agents including anaerobes (4.2%), complicated hydatid cyst (2.5%), *Influenza A* virus (4.2%; including 2 cases of mixed *Influenza A*-bacterial infection), and *Klebsiella pneumoniae*, *Brucella melitensis*, *Mucor*, and varicella, each in 0.8% of the patients. The diagnosis of pneumonia remained unknown in 49 (40%) patients.

Conclusions: Tuberculosis was an important cause of CAP in our region. Hence, it should be considered in all patients admitted with a CAP diagnosis.

Keywords: Pneumonia; Etiology; Tuberculosis; *Streptococcus pneumoniae*

1. Background

In 1901, Sir William Osler noted in the fourth edition of his book, the principles and practice of medicine, that "the most widespread and fatal of all acute diseases, pneumonia, is now Captain of the Men of Death." Over a century later, the prominence of pneumonia as a clinical entity remains (1). Nowadays, it is the third most common cause of death in the world accounting for 7% of the total mortality of 56 million people. According to The world health organization (WHO) data, 3 - 4 million people die due to pneumonia, a large proportion of whom are children or elderly (2). Mortality is highest for CAP patients who require hospitalization, with a 30-day mortality rate of up to 23% in such patients. It has also been shown that all-cause mortality in patients with community-acquired pneumonia (CAP) is as high as 28% within one year (3).

It is often difficult to determine the microbiological cause of pneumonia. A microbiological diagnosis is confirmed in about 60% of the cases of CAP in research studies that use specialized tests to detect various pathogens but in only about 20% of the cases in everyday practice (4). Despite geographical variations, *Streptococcus pneumoniae* is the most common cause of pneumonia worldwide (4). The rank order of the most common causes of pneumonia varies according to the severity of the illness. Therefore, when considering the etiology of CAP, it is useful to categorize patients into those who can be treated on an ambulatory basis, those who require hospitalization, and those who require admission to an intensive care unit (ICU) (5). There is a dearth of research on the etiology and prevalence of CAP in Iran. Our review of the published and unpublished literature to identify studies on CAP in Iran yielded only a few studies that evaluated the etiological diagnosis of CAP in adults, most of them including only one or two pathogens.

2. Objectives

The present prospective observational study is an etio-

logical survey of CAP during a period of 12 months in the Iranian city of Mashhad. To our knowledge, this is one of the first prospective hospital-based studies to comprehensively evaluate the epidemiological, demographical, clinical, and prognostic factors of patients with CAP in Iran.

3. Patients and Methods

The study was prospective and observational.

3.1. Selection and Description of Participants

We included in this study nearly all adult patients (aged ≥ 16 years) admitted to Imam Reza Hospital, a 1000-bed university hospital in Mashhad, Iran, between February 2013 and January 2014, with the diagnosis of CAP. The exclusion criteria comprised history of transplantation, recent chemotherapy with/without iatrogenic neutropenia within the previous 3 months, pneumonia caused by hospitalization or within the previous 3 months, chronic pneumonia (> 4 weeks), and refusal to sign the informed consent form. Out of 166 patients with community-acquired lower respiratory tract involvement with chest infiltrates, 140 cases were eligible for this study. Twenty patients with lower respiratory symptoms and infiltrates on chest radiography with an emerging alternative/non-infectious diagnosis during the follow-up (e.g. pulmonary emboli or malignancy) were secondarily excluded.

Statistical analyses were only performed on the remaining 120 patients with the diagnosis of acute CAP with an infectious etiology after the secondary exclusion. Clinical, radiological, and microbiological data of the patients were collected. Elderly was defined as persons aged ≥ 65 years. Chronic obstructive pulmonary disease (COPD) was defined clinically as the presence of a chronic productive cough for ≥ 3 months during each of 2 consecutive years (other causes of cough being excluded). Bedridden status was defined as confined to bed by sickness or old age. Opium addiction was defined by behaviors that included one or more of the following: impaired control over drug (opioid) use; compulsive use; continued use despite harm; and craving. The patients gave written informed consent, and the study was approved by the Ethics Committee of Mashhad University of Medical Sciences (Code: 900983).

3.2. Technical Information

The diagnostic criteria for CAP included an infiltrate on chest radiograph in a patient with either fever or clinical signs/symptoms of the lower respiratory tract infection, or both. Pneumonia was defined as acute if the symptoms lasted < 4 weeks. Parapneumonic effusion was defined as exudative pleural effusion associated with lung infection, i.e. pneumonia. According to Light's traditional criteria, if at least one of the following three criteria was present, the fluid was defined as exudates:

A. Pleural fluid protein/serum protein ratio > 0.5;

B. Pleural fluid lactate dehydrogenase (LDH)/serum LDH ratio > 0.6; and

C. Pleural fluid LDH > two-thirds the upper limits of the laboratory's normal serum LDH.

The sputum specimens were sent to the microbiological laboratory and processed immediately. No special procedures were performed to obtain sputum samples if they could not be obtained spontaneously except for endotracheal aspiration for the patients with early endotracheal intubation. A Gram stain was performed on a purulent portion of each sputum specimen. The sputum samples were considered of good quality if they had < 10 squamous cells and > 25 leukocytes per low-power field. Otherwise, the sputum sample was considered contaminated by saliva and rejected. The good quality specimens were then screened for a predominant bacterial morphological type in an oil-immersion field. Only the good quality specimens were used to culture the bacteria. The sputum specimens were also stained using Ziehl-Neelsen staining for the detection of mycobacteria. Blood for culture was inoculated in standard BACTEC™ Plus Aerobic/F bottles (Becton Dickinson, Ireland).

The unconcentrated urine samples were tested with the immunochromatographic assays BinaxNOW® *S. pneumoniae* antigen (Binax, Maine, U.S.A.) and BinaxNOW® *Legionella pneumophila* antigen (Binax, Scarborough, Maine, U.S.A.) for the detection of *S. pneumoniae* antigen and *L. pneumophila* serogroup 1 antigen, respectively. *Legionella* spp. was evaluated by urinary antigen testing only, but not by culture or polymerase chain reaction (PCR).

In our study, diagnostic tests for *Mycoplasma pneumoniae*, *Chlamydophila pneumoniae*, *Chlamydophila psittaci*, and *Coxiella burnetii* were not used. Viral etiology was not evaluated except for influenza. In the case of varicella pneumonia, the presumptive diagnosis was based on the compatible clinical and radiological manifestations of pneumonia and the presence of characteristic vesicular rash. PCR for the influenza virus was performed on nasopharyngeal swab specimens only in the patients with compatible clinical and epidemiological findings with or without a bacterial etiology confirmed by rapid tests, reverse transcription polymerase chain reaction (RT-PCR) with the Qiagen one-step real-time. The detection kit was used for the purification and detection of the influenza virus. The procalcitonin (PCT) levels were determined using a semi-quantitative solid-phase immunoassay (B.R.A.H.M.S. PCT-Q, B.R.A.H.M.S.-Diagnostica GmbH, Hennigsdorf, Germany) on 200 μL plasma. The PCT levels were categorized into four groups (i.e. < 0.5 μg/L, 0.5 - < 2 μg/L, 2 - <10 μg/L, and ≥10 μg/L) according to the provided reference scale. The test was performed within the first 12 hours of patient admission.

The etiology of CAP was classified as definitive if one of the following criteria was met: 1. Identification of an etiological agent from blood or pleural fluid; 2. Detection of the *S. pneumoniae* antigen or *L. pneumophila* antigen in urine; 3. Detection of the influenza virus from a nasopharyngeal sample by PCR; and 4. One or more initial sputum smear examinations positive for acid-fast bacilli

(AFB) or positive PCR for *Mycobacterium tuberculosis* on body fluids. *M. tuberculosis* DNA was extracted from the clinical samples using an *M. tuberculosis* Real-Time PCR Kit (Rotor-Gene™ 3000 (Corbett Life Science)).

The etiology of pneumonia was defined as presumptive when the identification of the etiological agent was based on: 1. Predominant organism in a good quality sputum sample Gram staining (defined as an average of >10 organisms of proper structure per oil-immersion field, > 75% of organisms on the slide of proper structure, or when either of these two criteria was met) and a positive sputum culture. 2. Patients in whom the Gram staining of the sputum revealed a mixed flora with the accompanying foul smell of the sputum were defined as having presumptive aspiration pneumonia with polymicrobial agents, including anaerobic organisms. 3. Clinical, laboratory, and radiological findings compatible with pulmonary tuberculosis with no response to the empirical antibiotic therapy and other etiological agents as the cause of clinical syndrome were ruled out; but *M. tuberculosis* was not isolated.

3.3. Statistics

The statistical analyses were performed using Statistical Package for the Social Sciences (SPSS) and the R programming language. The discrete variables are expressed as counts (percentage) and the continuous variables as mean ± standard deviation (SD), unless stated otherwise. Frequency comparison was done via the χ^2 test or the Fisher exact test for the categorical variables and the Student t-test or the Mann-Whitney U test for the continuous variables. A P value < 0.05 was considered significant.

4. Results

The 120 patients with the diagnosis of acute CAP with an infectious etiology were comprised of 76 (63.3%) males and 44 (36.7%) females. The mean age of the study population was 50.4 ± 22.6 years (17 - 94). The patients' ages were not normally distributed. More than one-third (35.8%) of all the patients hospitalized for CAP were elderly, 46.5% of whom were > 75 years old. The male-to-female ratio was 1.7. However, the trend of more male subject enrolment was not seen across all the age groups. The most common clinical findings were cough in 85% (n = 102) and fever in 83.3% (n = 100) of the patients, followed by sputum production 52% (n = 62), dyspnea 77.5% (n = 93), altered mental status 32.5% (n = 39), chest pain 18.3% (n = 22), hemoptysis 13.3% (n = 16), nausea/vomiting 13.3% (n = 16), diarrhea 5.8% (n = 7), myalgia 20.8% (n = 25), and weight loss 15.8% (n = 19). Of the 120 patients in our study, 66 (55%) cases had classic lobar pneumonia on chest radiography. Less common radiographic findings included bronchopneumonia in 30 (25%), cavitary lung lesion(s) in 13 (10.8%), diffuse interstitial/reticular infiltrates in 11 (9.1%), necrotizing infiltrates in 10 (8.3%), micronodular infiltrates in 5 (4.1%), and mixed infiltrates in 10 (8.3%) patients. Sixty-seven (55.8%) patients had bilateral involvement on chest radiography.

The most common underlying diseases in the patients were COPD (18.3%), diabetes mellitus (6.6%), and bedridden status (6.6%). Two patients with CAP were diagnosed to have HIV infection, and one patient who presented with community acquired non-responding pneumonia of 3 weeks' duration was finally diagnosed as a case of pneumococcal pneumonia in the setting of common variable immunodeficiency. The most common etiological diagnosis was *S. pneumoniae* (24.4%), followed by *M. tuberculosis* (17.5%), *S. aureus* (6.7%), polymicrobial agents including anaerobes (4.2%), complicated hydatid cyst (2.5%), *Influenza A* virus (4.2%) (including 2 cases of mixed *Influenza A*-bacterial infection), and *Klebsiella pneumoniae*, *Brucella melitensis*, *Mucor*, and varicella, each in 0.8% of the patients. The diagnosis of pneumonia remained unknown in 49 (40%) patients (Table 1).

Table 1. Frequency of the Microbiological Diagnoses in the Patients With Community-Acquired Pneumonia [a]

Etiological Agent	Definite [b]	Presumptive	Total [c]
S. pneumoniae	25	4	29 (24.4)
M. tuberculosis	19	2	21 (17.5)
S. aureus	6 [d]	2	8 (6.7)
K. pneumoniae	-	1	1 (0.8)
B. melitensis	1	-	1 (0.8)
Polymicrobial including anaerobes	-	5	5 (4.2)
Mucor	1	-	1 (0.8)
Influenza A	5 [d]	-	5 (4.2)
Varicella	-	1	1 (0.8)
Complicated hydatid cyst	3	-	3 (2.5)
L. pneumophila	0	-	0
CAP of Unknown Etiology (CAPUE) but responsive to antibacterial therapy	-	48	49 (40)
With serum PCT > 0.5	-	35	35 (71.4)
With serum PCT < 0.5	-	14	14 (28.5)
Total	57	63	120 (100) [d]

[a] Abbreviations: CAP: Community-Acquired Pneumonia, PCT: Procalcitonin.
[b] Pneumococcal CAP was diagnosed exclusively by the urinary antigen test in 9 (31%) cases.
[c] Values are presented as No. (%).
[d] Two cases had mixed infection with influenza virus and *S. aureus*.

The patients with community-acquired pneumonia of unknown etiology (CAPUE) were classified into two groups: 1) CAPUE with PCT ≥ 0.5 ng/mL (71.4%) and 2) CAPUE with PCT < 0.5 ng/mL (28.5%). Among the patients with pulmonary tuberculosis, 3 had concomitant tuberculous meningitis, which was confirmed by positive cerebrospinal fluid PCR for *M. tuberculosis*. All of them had a miliary pattern on chest radiography. Additionally, the usefulness of the sputum Gram stain in guiding the etiological diagnosis was assessed. Sixty-one per cent of the patients had some type of respiratory specimens, including good quality sputum, endotracheal tube aspirate, and/or pleural effusion for Gram staining and culture. For the patients with the definite diagnosis of pneumococcal pneumonia (25 patients), the Gram stain suggested pneumococcal infection in 17 (65.3%). The blood cultures were positive in 4 (3.33%) of the 120 patients. Parapneumonic effusions were observed in 30.8% of the patients. The frequency of parapneumonic effusions was 33.3% in pneumococcal pneumonia, 62.5% in staphylococcal pneumonia, and 20.4% in the patients with CAPUE. Pleural effusion was detected in 38.1% of the patients with tuberculosis. The only case of brucella pneumonia was complicated with loculated parapneumonic effusion.

The overall in-hospital mortality (IHM) rate was 23.6%. The rate was 33.3% among the elderly patients compared with the younger adults, with a 20.3% death rate, which was higher, but not statistically significant (P = 0.14). The 3-day mortality rate was 3.3%. Intensive vasopressor and respiratory support (IVRS) was required in 38 (36.1%) patients, 16 (42.1%) of whom did not receive IVRS in the first 24 hours post admission. The study population included 46 (38.7%) opioid addicts. The frequency distribution of the etiological organisms among this group of CAP patients was as follows: *S. pneumoniae* 16 (34.8%); *Mycobacterium* 11 (23.9%); *S. aureus* 4 (8.7%); polymicrobial agents including anaerobes 1 (2.2%); varicella 1 (2.3%); complicated hydatid cyst 1 (2.3%); and CAPUE but responsive to antibacterial therapy 11 (24.5%).

As was mentioned earlier, more than one-third of our patients were elderly. The frequency distribution of the etiological organisms among the elderly patients with CAP was as follows: *S. pneumoniae* 14 (32.6%); *Mycobacterium* 5 (11.6%); *S. aureus* 5 (11.6%); *K. pneumoniae* 1 (2.3%); polymicrobial agents including anaerobes 3 (7.1%); mucormycosis 1 (2.4%); *Influenza A* 1 (2.4%); complicated hydatid cyst 1 (2.4%); and CAPUE but responsive to antibacterial therapy 16 (37.3%). The etiological diagnosis remained unknown in 37.3% of the elderly patients, which was lower than that in the younger adults, but the difference was not statistically significant (39% vs. 49.1%, P = 0.829). A comparative analysis between these two age groups revealed that the duration of clinical symptoms before admission was significantly lower (7.6 ± 4.4 vs. 11.1 ± 7.7 days, P = 0.016) and the presence of underlying diseases (P < 0.001) and altered mental status on admission (P = 0.003) was more frequent in the elderly patients. The IHM rate and the number of the patients who needed IVRS were higher in the patients ≥ 65 years compared with the younger adults; nevertheless, these differences were not statistically significant (P = 0.063 and 0.242, respectively) (Table 2).

Table 2. Comparison Between the Different Characteristics of the Elderly and Young Adults With Community-Acquired Pneumonia [a,b]

Patients' Characteristics	Elderly	Young Adult	P Value
Age, y	75.9 ± 7.4	36.1 ± 13.1	0.001
Duration of symptoms	7.6 ± 4.4	11.1 ± 7.7	0.016
Underlying diseases	29 (67.4)	25 (32.9)	0.001
Addiction	13 (30.2)	33 (43.4)	0.156
Bedridden Status	6 (14)	2 (2.6)	0.047
Altered mental status	21 (50)	17 (23)	0.003
Hypotension	9 (23.7)	14 (19.7)	0.62
Tachycardia	31 (83.8)	61 (84.7)	0.898
Tachypnea	35 (92.1)	61 (83.6)	0.212
High-grade fever	26 (68.4)	54 (76.1)	0.39
Severe hypoxia	17 (44.7)	31 (43.7)	0.914
Pleurisy	9 (29)	19 (30.6)	0.53
Bilateral involvement	18 (43.9)	44 (62)	0.064
IVRS requirement	16 (39)	21 (28.4)	0.242
Mechanical ventilation after 24h of admission	8 (19.5)	8 (10.7)	0.187
In-hospital mortality	14 (33.3)	14 (18.2)	0.063

[a] The values are presented as mean ± standard deviation or No (%).
[b] Abbreviation: IVRS, Intensive Vasopressor or Respiratory Support.

5. Discussion

In this study, we evaluated the frequency of the microbiological etiology of CAP in adult patients who required hospital admission during a period of 12 months. We found that *S. pneumoniae* was the most common etiological agent of CAP (24.4%). This result chimes in with previous studies that showed this organism as the most common etiology of CAP with a frequency of 10% to 20% (6). Identifying the cause of CAP remains a challenge. Concordant with some previous studies, we could not diagnose the etiology of CAP in a significant number of the patients (40.4%), 69.6% of whom had PCT > 0.5 ng/mL. It has been previously demonstrated that the PCT level is lower in pneumonia caused by viral and atypical pathogens than a typical bacterial etiology (7, 8). It can be postulated, but not documented, that 31.4% of the patients with CAPUE and PCT levels < 0.5 ng/mL might have had an atypical or viral etiology. The other causative agents among our patients included *M. tuberculosis*, *S. aureus*, polymicrobial agents including anaerobes, complicated hydatid cyst, *Influenza A* virus, *K. pneumoniae*, *B. melitensis*, *Mucor*, and varicella.

The use of blood and pleural culture in the etiological diagnosis of CAP has been hampered by the limited sensitivity. Bacterial pneumonia may have been underestimated in our study due to the low rate of the bacteremic cases and the low number of the positive cultures with a definitive diagnostic value in the non-tuberculous patients with CAP (3.33% and 8%, respectively). Previously, the diagnostic yield of blood culture was reported at < 10% (9, 10). In a study conducted by Benenson et al. (9), three factors were associated with positive blood cultures: oxygen saturation < 90%; serum sodium < 130 mEq/L; and respiratory rate > 30 breaths/minute.

The authors suggested that although the sensitivity of the pneumococcal urinary antigen test is lower in patients who are not bacteremic, the presence of a positive urinary antigen test in a non-bacteremic patient can be helpful for tailoring therapy. The main disadvantage of this test is its false-positive results in the case of nasopharyngeal colonization, especially in children or in patients with recent episodes of pneumococcal infection. However, because of the exclusion criteria of our study, this problem was not of significance.

This finding is in contrast to the results of some previous studies that demonstrated a frequency of 6% to 13% for *L. pneumophila* in patients with community-acquired and nosocomial pneumonia in different parts of Iran (13-18) and up to 22.1% in pregnant patients with CAP (19). Additionally, several studies have documented the contamination of different water sources with *Legionella* in our country (20-22). The detection of the *L. pneumophila* antigen by the immunochromatographic assay had optimum sensitivity for the detection of *L. pneumophila* serogroup 1. However, most evidence shows that *L. pneumophila* serogroup 1 is the etiological agent of 70% of the community-acquired Legionnaires' disease in most parts of the world (23, 24). Accordingly, it can be suggested that *L. pneumophila* is not an important and prevalent etiological cause of CAP in our region, compared to other microorganisms. In a study performed in Japan, the incidence of *L. pneumonia* was also far lower than that in Western countries (25).

The sensitivity and specificity of the sputum Gram stain vary substantially in different settings. The sensitivity of the Gram stain compared to culture ranges between 15% and 100% and its specificity ranges from 11% to 100% (11). Of the 29 patients in our study with the diagnosis of pneumococcal pneumonia, the etiological diagnosis of 8 (27.5%) cases was only documented based on a positive *S. pneumoniae* urinary antigen test. The important role of this assay in the rapid etiological diagnosis of CAP could not be overemphasized, especially in patients who cannot produce good quality sputum, those who are not bacteremic, and those with the administration of antibiotics before admission. Sorde et al. (12) studied adult patients hospitalized with CAP caused by *S. pneumoniae* and diagnosed pneumococcal CAP exclusively by the urinary antigen test in 44%.

The estimates of Legionnaires' disease as a cause of CAP requiring hospitalization in adults range from 0.5% to 10% of all admitted pneumonia cases; an average value is probably about 2%, even in geographical regions with excellent diagnostic capabilities (1). Although we tested all the patients' urine samples with the immunochromatographic *Legionella* urinary antigen assay, *L. pneumophila* was detected by the urinary antigen in no patients in our study.

The most common underlying conditions in our patients with CAP were age ≥ 65 years, COPD, diabetes mellitus, and bedridden status. Elderly, defined as persons aged ≥ 65, accounted for more than one-third of all the patients hospitalized for CAP in our study. The most common organisms isolated in this age group were *S. pneumoniae*, *M. tuberculosis*, and polymicrobial agents including anaerobes, respectively. Additionally, the etiological diagnosis was not identified in 37.3% of these patients. Previously, the importance of *S. pneumoniae* as a cause of CAP in the elderly has been documented (26). Hashemi et al. (27) compared the frequency of the bacterial agents of CAP between elderly individuals and younger adults admitted to hospital and found that *S. pneumoniae* was the most frequent pathogen of CAP in the elderly patients, followed by *S. aureus* and *Pseudomonas aeruginosa*.

According to some previous studies, the mortality rate among hospitalized CAP patients is less than 15%. The overall IHM rate was 23.6% in our patients, which is high compared with the previously reported rates (28, 29). It has been demonstrated that the first days of admission are associated with the highest mortality (29). Early mortality has been attributed to respiratory failure (30). In contrast, only 4.2% of the IHM occurred within the first

3 days (3-day mortality) in our study. Halm et al. (31) demonstrated that the initial severity of pneumonia correlated with the number of days until clinical stability. On the other hand, Menendez et al. (32) reported that adherence to antibiotic guidelines was associated with earlier clinical stability. Once a patient's condition becomes stable, the risk of serious clinical deterioration is 1% or less (31). In contrast, the highest incidence of IHM in our study occurred after the first day and a significant number of IVRS requirements happened after the first 24 hours of hospitalization. This finding could be a reflection of delayed clinical stability in our patients. Therefore, the difference in the distribution of hospital deaths over time in our study compared with some previous studies could have several possible explanations, including patient-related, pathogen-related, and/or management-related factors.

Among hospitalized patients, mortality rates are higher in patients with severe pneumonia, especially in those requiring treatment in an ICU. In a meta-analysis by Fine et al. (28), the mortality of the CAP patients treated in an ICU was 37%. It has been mentioned that since the criteria for ICU admission vary both between hospitals and between countries, assessing IVRS rather than simple ICU admission may be more useful in evaluating the severity of pneumonia because it is probably a more objective marker of CAP severity across institutions and health care systems (33). According to some previous studies, about 10% - 20% of hospitalized patients with CAP require IVRS (33-35), whereas more than one-third (36.1%) of our patients needed IVRS. Accordingly, our patients presented with more severe illness. However, only 57.9% of these requirements occurred within the first 24 hours.

Mortality is also higher among elderly patients (14% - 18%) (28, 29, 36). It has also been demonstrated that in the hospitalized elderly, CAP is a common and frequently fatal disease that often requires ICU admission and mechanical ventilation and consumes considerable health care resources (37). In our study, the IHM rate was 33.3% among the elderly patients compared with the younger adults, with a 20.3% death rate, which was higher, but not statistically significant (P = 0.14). The mean length of stay (LOS) in hospital was longer and the number of the cases who needed IVRS was higher among the elderly patients compared with the younger adults. Underlying diseases, including bedridden status, were also more common in the older patients.

In conclusion, although *S. pneumoniae* is the most common cause of CAP in many countries, there are considerable geographic differences in the incidence of other pathogens. Tuberculosis is an important cause of CAP in our region, and this diagnosis should be considered in all patients who present with CAP. It can also be suggested that *L. pneumophila* is not an important and prevalent etiological cause of CAP in our region, compared to other microorganisms. Age $\geq$ 65 years accounted for approximately one-third of the patients with higher IHM, longer LOS, and more frequent underlying diseases.

Acknowledgements

This article was derived in part from a thesis (# 2799-T) written by Fereshte Sheybani for specialty in infectious diseases. This study was approved by the ethics committee of Mashhad University of Medical Sciences (Code: 900983).

Authors' Contributions

Hamidreza Naderi, Fereshte Sheybani, Mohammadreza Sarvghad, and Zahra Meshkat contributed in designing, data gathering, writing, and editing the manuscript and Mehdi Jabbari Nooghabi contributed in designing the manuscript and statistical analysis.

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