Prognostic factors and outcome of patients hospitalized with community acquired Pneumonia

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Introduction
Community acquired Pneumonia (CAP) is defined as lung infection acquired from community. Despite advances in diagnosis and treatment of Pneumonia, it is still considered as an important mortality and morbidity factor.1-3

Annually, in the United States (US), average of 5 to 6 million people are infected by CAP, and more than 1 million of them require hospitality. About 10%-20% of patients with CAP need hospitalization in intensive care unit (ICU), and about 20%-50% of them finally die.5,6 Prevalence of this disease has been estimated as 14 cases per 1000 people annually.7

The most prevalence of CAP is in children under 5 years old and elderly people over 75 years old. The prevalence of this disease could be 5 times higher in developing countries compared with developed countries.8 In the US, economic burden of CAP has been reported as 17 milliard dollars, and also in the developed countries more than half of the CAP hospitalizations happen in people over 65 years old, and oldness is
one of the main reasons of mortality and morbidity in this disease. Some risk factors have been mentioned such as age over sixty, alcoholism, cardiac diseases, other comorbid lung diseases, immunosuppressive therapies, smoking, history of Pneumonia and previous respiratory infection, low body mass index (BMI), asthma, and diabetes mellitus (DM). In diagnosing of the disease, clinical symptoms as well as radiographic evidence of lung and leukocytosis are important. In old people symptoms are non-specific. While the disease is diagnosed, empirical treatment should be immediately implemented. Delay more than 4 hours in initiating therapy increases risk of mortality. Treatment duration changes between 7 to 21 days based on severity of disease and probable pathogen. In old patients with comorbidity, longer treatment takes place. Using pneumococcal vaccine has been advised in specific conditions, since 95% of Pneumonia are resulted from streptococcus pneumonia. Considering improvements in production of vaccine, and efforts in reducing smoking, now this microorganism is the cause of 10%-15% of CAP outpatients. Of course various bacterial, viral, and fungal factors could be the cause of CAP. In determining disease severity, different scales such as Pneumonia Severity Index (PSI) are used. CURB-65 is other scale which is used, and mortality with tachypnea, diastolic pressure under 60 mmHg, and urea over 7 mmol/l are independent factors related to mortality in CAP. This association has not been approved in other studies. In our study, independent prognostic factors associated with mortality included pleuritic chest pain, changes in the level of consciousness, vital signs, and neoplastic diseases. In a study conducted in Spain, pulmonary infiltration in the first 48 hours has been reported as bad prognostic factor.

Considering high prevalence of CAP and importance of mortality prognostic factors, and for reducing health and mortality costs of this disease, the current study has been conducted in infectious centers of Tabriz University of Medical Sciences, Tabriz, Iran, in order to investigate patients with CAP, prognostic factors, and their clinical outcomes.

**Methods**

In a descriptive-analytical study, 236 patients with CAP diagnosis, hospitalized in infectious centers of Tabriz University of Medical Sciences during two years of 2012-2013, were randomly chosen based on file numbers and included into the study. Inclusion criteria were: existence of acute respiratory symptoms (fever, cough, sputum, shortness of breath), existence of physical findings (tachycardia, tachypnea, dullness in percussion, consolidation evidence, and crackles), and existence of radiologic findings in chest radiography.

Exclusion criteria were: similar situations that arise in the differential diagnosis (thromboembolism, pulmonary edema, heart failure (HF), chronic Pneumonia), and inadequate information. Questionnaire was completed for all patients based on their file information including demographic information (age, sex, history of stay in sanitarium, smoking, alcohol use, drugs use), comorbidities, recent antibiotic therapy, laboratory parameters such as arterial blood gas (ABG), urea, creatinine, white blood cell (WBC) count, sodium, hematocrit, blood culture results, and other sterile areas), graphic findings of chest, length of stay, and final result of the disease. After collecting primary information, data were finally processed in SPSS software (version 12, SPSS Inc., Chicago, IL, USA) and underwent statistical analysis. Obtained information was presented as mean ± standard deviation (SD), frequency, and percentage. In order to compare qualitative variables, chi-square test has been used, and to compare quantitative variables independent t-test was applied. To investigate correlation between variables, Pearson coefficient (r) was calculated. In all steps of study, results were considered statistically significant when P ≤ 0.05.
Results
Of 236 investigated patients, 117 patients (49.6%) were men, while 119 patients (50.2%) were women. Mean age of the patients was 68.7 ± 18.9 years. There was no significant difference between men and women in terms of developing CAP (P = 0.660). Of 236 patients, 171 cases (72.5%) were smokers, and mean cigarette consumption was annually 23.73 ± 11.97 pockets. Only 8 patients (3.4%) had history of alcohol drinking and 20 patients (8.5%) had addiction or history of addiction.

Table 1 shows the comparison of laboratory findings in dead and discharged patients. Table 2 shows the correlation of investigated variables with mortality increase. Table 3 shows the relationship between hospitalization days and sex, and the final results of the patients.

Table 1. Comparison of laboratory findings in dead and discharged patients with community acquired Pneumonia (CAP) hospitalized in infectious centers of Tabriz University of Medical Sciences, 2012-2013

<table>
<thead>
<tr>
<th>Test parameter</th>
<th>Patients</th>
<th>Discharged</th>
<th>Passed away</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Urea (mean ± SD)</td>
<td>31.68 ± 2.19</td>
<td>47.41 ± 8.95</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>Serum creatinine (mean ± SD)</td>
<td>1.33 ± 0.38</td>
<td>2.13 ± 1.56</td>
<td></td>
<td>0.004</td>
</tr>
<tr>
<td>Sodium (mean ± SD)</td>
<td>134.65 ± 3.62</td>
<td>129.96 ± 3.33</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>pH (mean ± SD)</td>
<td>7.38 ± 0.04</td>
<td>7.38 ± 0.06</td>
<td></td>
<td>0.246</td>
</tr>
<tr>
<td>Hematocrit (mean ± SD)</td>
<td>40.45 ± 4.10</td>
<td>34.16 ± 3.57</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>WBC (mean ± SD)</td>
<td>12117.75 ± 3422.81</td>
<td>10739.28 ± 5179.25</td>
<td></td>
<td>0.001</td>
</tr>
<tr>
<td>PCO₂ (mean ± SD)</td>
<td>38.94 ± 7.42</td>
<td>34.14 ± 5.69</td>
<td></td>
<td>0.001</td>
</tr>
</tbody>
</table>

SD: Standard deviation; WBC: White blood cell; PCO₂: Partial pressure of carbon dioxide

Table 2. Correlation (r) of investigated variables with mortality increase in patients with community acquired Pneumonia (CAP) hospitalized in infectious centers of Tabriz University of Medical Sciences, 2012-2013

<table>
<thead>
<tr>
<th>Investigated variable</th>
<th>Correlation coefficient (r)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood urea increase</td>
<td>0.271</td>
<td>0.001</td>
</tr>
<tr>
<td>Blood creatinine level increase</td>
<td>0.226</td>
<td>0.001</td>
</tr>
<tr>
<td>WBC decrease</td>
<td>0.124</td>
<td>0.058</td>
</tr>
<tr>
<td>Respiratory rate increase</td>
<td>0.154</td>
<td>0.018</td>
</tr>
<tr>
<td>Heart rate increase</td>
<td>0.406</td>
<td>0.001</td>
</tr>
<tr>
<td>Body temperature decrease</td>
<td>0.064</td>
<td>0.331</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td>0.313</td>
<td>.001</td>
</tr>
<tr>
<td>Incomplete antibiotic therapy</td>
<td>0.103</td>
<td>0.113</td>
</tr>
</tbody>
</table>

WBC: White blood cell

Discussion
Despite developments in diagnosis and treatment of CAP, it is still considered as an important mortality and morbidity factor in the world; and in spite of various studies in this field, some prognostic factors of CAP are not still identified and reported. Based on the current study, 236 patients with CAP were randomly included into a descriptive-retrospective study. Male to female ratio was approximately 1 (1 to 1.02), and mean age was 68.7 ± 18.9 years. Of samples, 72.5% were smokers, 3.4% had alcohol consumption history, and 8.5% had history of addiction. About comorbid diseases, the most prevalent one was history of lung diseases with 36.4% followed by heart diseases (27.1%), and DM.

Of the 236 investigated patients, 12 patients (5.1%) had renal problems, 4 patients (1.7%) had liver disease, 57 patients (24.2%) had aspiration history, 86 patients (36.4%) had lung disease, and 23 patients (9.7%) had previous Pneumonia history. In this study, final results of the patients had no significant relationship with systolic blood pressure (P = 0.501, r = 0.035) and with diastolic blood pressure (P = 0.208, r = 0.082).
(24.2%). In radiographic study, there was pleural effusion in 24.2%, and also 36.4% had undergone incomplete antibiotic therapy. 9.7% of patients were hospitalized in ICU, and mortality rate was 11.9%. While investigating the relationship between prognostic factors and mortality rate of patients, it was found that increase in heart rate ($r = 0.406$), pleural effusion ($r = 0.313$), increase in blood urea level ($r = 0.271$), and increase in blood creatinine level ($r = 0.226$) were respectively effective factors in mortality rate of patients, and were statistically significant ($P < 0.050$). However, there was a relationship between previous history of incomplete antibiotic therapy and decrease in WBC number on one hand and mortality rate of patients on the other hand; this relationship was not statistically significant ($P > 0.05$).

In a study, Vila-Corcoles et al. investigated 11241 old people, aiming at investigating incidence, etiology, and clinical symptoms of patients with CAP. Duration of this cohort study was 40 months, and research sample was selected from 8 centers in Spain. 44.5% of the patients were men and 55.5% were women. The most comorbidity was DM (23.6%) followed by chronic cardiac diseases and chronic lung diseases. Results of the study showed that mean prevalence of CAP in people with normal immune system was 11.6 in 1000 persons, and that of people with a weakened immune system was 30.9 per 1000 people. The highest prevalence was for patients with chronic lung disease with 46.5 per 1000 people as well as patients with long-term treatment with corticosteroids with 40.1 per 1000 people. In etiology section of 358 studied patients, 131 patients showed diagnosable organism, where streptococcus has been the most prevalent agent organism. Mean hospitalization days of the patients was 10.4 days. 6.3% of the patients had pleural effusion and 2.5% had multi-lobar Pneumonia. Finally, having history of hospitalization due to CAP during the last 2 years, having chronic lung diseases, chronic cardiac and liver diseases, cancer, and corticosteroid treatments as well as age and male gender were reported as risk factors.

Further, in this study, the number of men and women was approximately the same (1 to 1.02). Mean days of hospitalization of the patients was $8.0 \pm 4.6$ days. Comorbidity of DM in this study was 24.2%, but the most prevalent comorbidity in the patients was lung diseases (36.4%). Considering retrospective nature of the study and problems related to isolation of organisms, investigating etiological factors was not completely possible and information registered in files of the patients was not complete in this regard.

In this field, Song et al. also conducted a study aiming at investigating epidemiology of CAP comorbid diseases. In this study, 955 patients from 8 Asian countries were studied. Results of the study showed that bronchopulmonary diseases (29.0%) are the most prevalent comorbid disease followed by cardiovascular diseases (CVDs) (19.9%), malignancies (11.7%), and neurological diseases (8.2%). Mortality rate has been reported as 7.3% and the most important statistically significant factors associated with mortality were: stay in a nursing home, mechanical ventilation and malignancies, CVDs, and respiratory rate over 30 per minute. In addition, in the present study comorbid lung diseases were the most prevalent comorbidity in the patients (36.4%) followed by cardiac diseases (27.1%). Moreover, based on the results of the current study, increase in creatinine level, respiratory rate, heart rate, and pleural effusion were statistically significant factors associated with increase in mortality rate of the patients. Finally, the mortality rate in this study was 11.9%.

Results of the study by Welte and Kohnlein, aiming at epidemiological investigation of CAP, showed that the mortality rate in outpatients is low (less than two percent), but this rate in patients hospitalized in ICU is more than 50%. Of important risk factors associated with mortality were: age over 65, male sex,
existence of comorbidities such as chronic heart diseases (CHDs), advanced chronic obstructive pulmonary diseases (COPDs), neurological diseases, and cirrhosis of the liver. Stay in nursing home and other care centers was also presented as one of the major causes of acquiring respiratory resistant infections.37

Fujiki et al. also conducted a study in Japan with the purpose of investigating mortality risk factors in patients with CAP. During this study, 208 hospitalized patients with CAP were studied. Results of this study showed that aspiration risk, low systolic blood pressure, advanced cardiac failure, and high Pneumonia score are of mortality-related risk factors in these patients.38

In a prospective study by Garbino et al., with the goal of epidemiological investigation of Pneumonia, 318 adult patients with CAP hospitalized in 7 medical centers were studied during two winters. Mean age of the patients was 70.4 years. Results of the study showed that in spite of high age, mortality rate has been only 8%, and underlying diseases in the patients included HF (23%), COPD (20%), renal failure (15%), and diabetes (12%).39

Conclusion
According to the results obtained, increase in heart rate (r = 0.406), pleural effusion (r = 0.313), blood urea level (r = 0.271), creatinine level (r = 0.226), and respiratory rate of patients (r = 0.154) had significant correlation with CAP-related mortality rate of patients. Lung disease, heart disease, and diabetes were the most common comorbid conditions in patients with CAP.

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Authors’ Contribution
All of the authors contributed equally.

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Conflict of Interest
Authors have no conflict of interest.

Ethical Approval
This study was approved by the Regional Medical Ethics Committee of Tabriz Branch, Islamic Azad University of Medical Sciences, under the number 10210101912019.

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