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British Journal of Medical and Health Research

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## Analysis of the In-hospital Mortality in Patients with Community-acquired Pneumonia

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### ABSTRACT

Community-acquired pneumonia (CAP) is a common disease with frequent hospitalization and still high mortality rate. The aim of the study is to analyze the clinical characteristics of patients who died in the hospital from CAP. 1292 patients hospitalized in the Clinic of Pneumonology and Phthisiatrics of MHAT “Saint Marina” – Varna were retrospectively studied for the period 2012 to 2015. Data were analyzed with statistical program SPSS.20. 148 patients (11.5%) died during the hospital stay. The non-survivors were significantly older than the survivors ( $67.6 \pm 14.2$  vs.  $58.9 \pm 17.1$  years,  $p < 0.001$ ). No significant difference in the mortality rate between male and female was proven (12.3 % vs. 10.3 %,  $p = 0.15$ ). Charlson comorbidity index was significantly higher in non-survivors compared to survivors ( $3.28 \pm 2.21$  vs.  $1.36 \pm 1.63$ ,  $p < 0.001$ ). Patients with dementia, carcinoma with metastases and cerebrovascular disease as concomitant comorbidities had the highest risk of dying in the hospital (OR 6.86 (3.97-11.84); 4.33 (1.43-13.12); 4.05 (2.77-5.92) resp.  $p < 0.05$ ). C-reactive protein was also significantly higher in non-survivors compared to survivors ( $171.85 \pm 83.17$  mg/L vs.  $123.42 \pm 99.68$  mg/L,  $p < 0.001$ ). The most common complication was acute respiratory failure (89.9%). Of the deceased patients 16.9% did not meet the criteria for severe CAP according to IDSA/ATS on admission. Most of the deceased patients (52%) died within the first 3 days of the hospital stay. Older patients with comorbidities had higher risk of dying in the hospital. Patients with CAP need intensified monitoring especially in the first 3 days even if they do not have severe pneumonia on admission.

**Keywords:** Community-acquired pneumonia, severity, mortality.

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Received 29 September 2017, Accepted 10 October 2017

## INTRODUCTION

Community-acquired pneumonia (CAP) is a common disease with frequent hospitalization and still high mortality rate. Despite the success of antibiotic treatment, the mortality rate ranges between 1-48%<sup>1</sup>. In developed countries, pneumonia and influenza are the leading cause for death from infectious diseases. In Bulgaria in 2016, mortality from pneumonia was 18.4/100 000 population, the rate increasing with age and in the age group over 85 years it reached 191.1/100 000 population<sup>2</sup>. Pneumonia is a socially significant disease associated with high morbidity, hospitalization and consumption of health resources. In European Union about 1 000 000 patients are hospitalized annually with CAP<sup>3</sup>. Taking into consideration the aging of the population and the increased comorbidity among the elderly, it can be expected that the incidence and mortality rate of pneumonia will remain high in the future. Several scales are used to determine the severity of pneumonia and the risk of mortality. The most widely used are PSI, CURB-65 and IDSA/ATS criteria<sup>4, 5, 6</sup>. Researchers still work on improving the identification of high-risk patients, and some biomarkers are being developed. Accurate identification of high-risk patients will support the development of therapeutic strategies to reduce mortality and improve prognosis.

### **Aim:**

To analyze the clinical characteristics of patients who died in the hospital from CAP.

## MATERIALS AND METHOD

1292 patients hospitalized in the Clinic of Pneumonology and Phthisiatrics of MHAT “Saint Marina” – Varna were retrospectively studied for the period 2012 to 2015. Patients were divided into two groups - survivors and non-survivors. The two groups were compared by demographic data and some basic characteristics of pneumonia. The deceased patients were analyzed by age, sex and concomitant diseases. Assessment of comorbidity was done by Charlson comorbidity index (CCI). The three major scales - PSI, CURB-65 and the IDSA/ATS criteria were used to assess the severity of pneumonia in deceased patients. Data were analyzed with statistical program SPSS.20. Descriptive, variance and comparative analyses were performed. To compare the groups T-test of Student and  $\chi^2$ -test were used. Quantitative variables were reported as mean value and standard deviation (mean  $\pm$  SD), and qualitative variables were reported as a count and relative share (%). Analysis of risk assessment (OR) was performed for evaluating the impact of comorbidities on the mortality.  $P < 0.05$  was accepted as statistically significant in all comparisons. The study was conducted in accordance with the Institutional Ethical Committee.

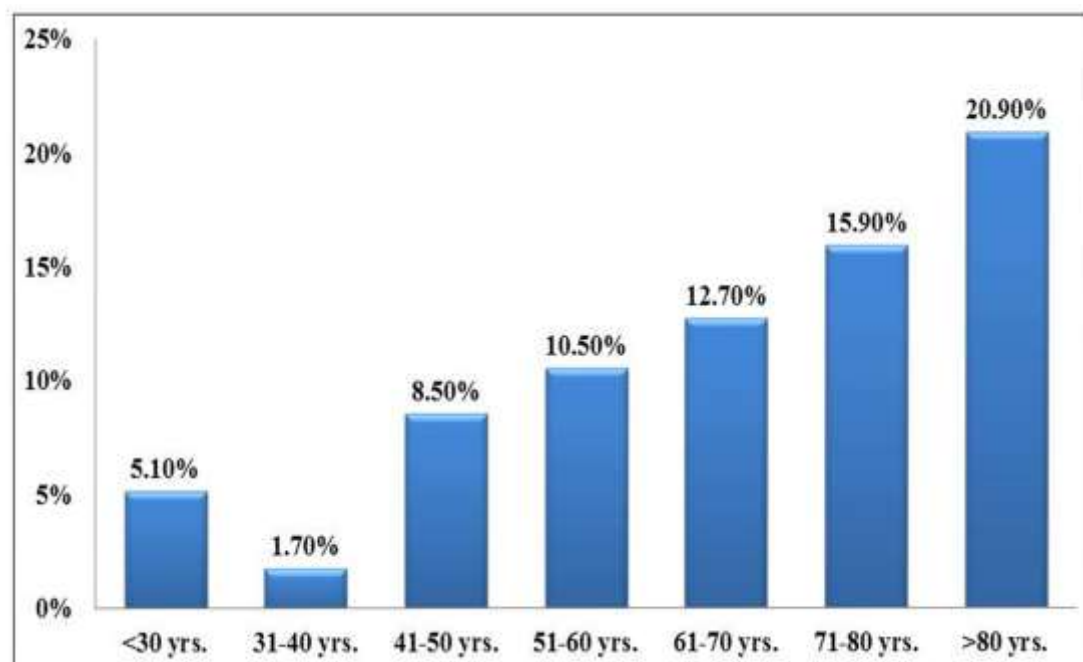
## RESULTS AND DISCUSSION

148 patients (11.5%) died during the hospital stay. The non-survivors were significantly older than the survivors ( $67.6 \pm 14.2$  vs.  $58.9 \pm 17.1$  years,  $p < 0.001$ ). No significant difference in the mortality rate between male and female was found (12.3 % vs. 10.3 %,  $p = 0.15$ ). Mortality in ICU is much higher than in general ward. Deceased patients had significantly higher CCI and C-reactive protein (CRP). The characteristics of the studied group are shown on tabl.1.

**Table 1: Characteristics of the studied group**

Characteristics	Survivors Number / %	Non-survivors Number / %	P-value
Age	1144 / 88.5%	148 / 11.5%	
Sex	$58.9 \pm 17.1$ years	$67.6 \pm 14.2$ years	$p < 0.001$
male	648 / 87.7%	91 / 12.3%	$p = 0.15$
female	496 / 89.7%	57 / 10.3%	
Site of care			
ICU-patients	145 / 54.3%	122 / 45.7%	$p < 0.001$
General ward	999 / 97.4%	26 / 2.6%	
Radiographic infiltrates			
monolobar	917 / 80.2%	64 / 43.2%	$p < 0.001$
multilobar	227 / 19.8%	84 / 56.8%	
Charlson comorbidity index (CCI)	$1.36 \pm 1.63$	$3.28 \pm 2.21$	$p < 0.001$
C-reactive protein	$123.42 \pm 99.68$	$171.85 \pm 83.17$	$p < 0.001$

We established a rise in mortality with increasing the age of patients. In the age group under 30 years it was 5.1%, in the age group 31-40 years it was only 1.7% and then it began gradually to increase and in the age group over 80 years it reached up to 20.9% (Fig.1)



**Figure 1: Percentage of deceased patients in different age groups**

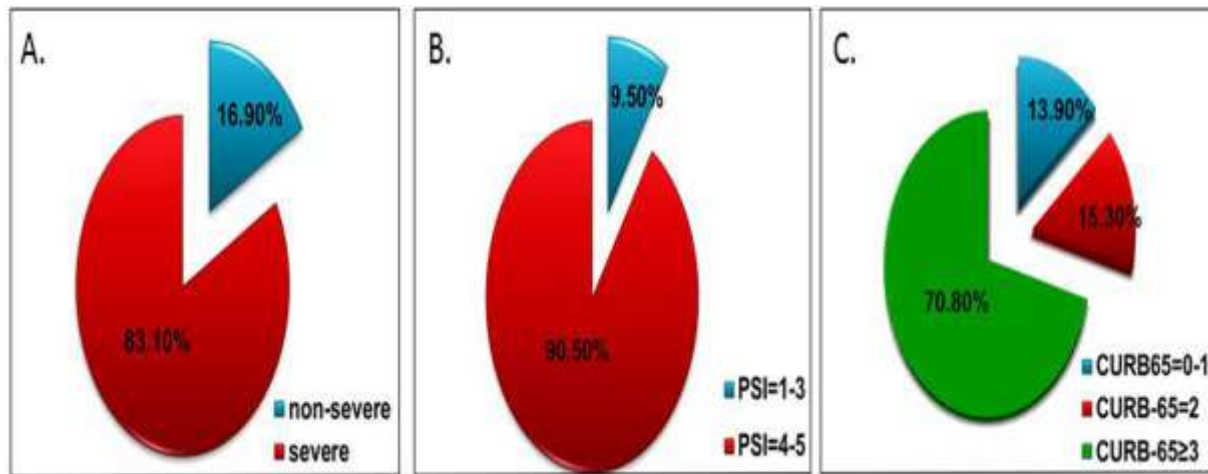
Comorbidity led to an increase of in-hospital mortality. While the mortality rate among patients without comorbidity was only 2.9%, the presence of at least one comorbidity increased the mortality to 15.8%. Patients with dementia, carcinoma with metastases and cerebrovascular disease as concomitant comorbidities had the highest risk of dying in the hospital (OR 6.86 (3.97-11.84); 4.33 (1.43-13.12); 4.05 (2.77-5.92) resp.  $p < 0.05$ ). Chronic renal failure, chronic liver disease, chronic heart failure, diabetes mellitus and ischemic heart disease also significantly increased the in-hospital mortality. Patients with malignant hemopathy, non-metastatic cancer, COPD, bronchial asthma, ulcer disease, peripheral vascular disease and connective tissue disease had not increased mortality risk (Tabl.2).

**Table 2: In-hospital mortality risk according to comorbidities**

Comorbidity	OR (95% CI)	p-value
Dementia	6.86 ( 3.97-11.84)	$P < 0.001$
Carcinoma with metastases	4.33 (1.43-13.12)	$P = 0.017$
Cerebrovascular disease	4.05 (2.77-5.92)	$P < 0.001$
Chronic renal failure	3.67 (2.35-5.73)	$P < 0.001$
Chronic liver disease	3.12 (1.70-5.71)	$P < 0.001$
Chronic heart failure	2.54 (1.76-3.67)	$P < 0.001$
Diabetes mellitus	2.41 (1.68-3.46)	$P < 0.001$
Ischaemic heart disease	2.22 (1.54-3.21)	$P < 0.001$
Malignant haemopathies	1.77 (0.72-4.38)	$P = 0.16$ (NS)
Ulcer disease	1.61 (0.79-3.25)	$P = 0.13$ (NS)
Peripheral vascular disease	1.54 (0.67-3.53)	$P = 0.21$ (NS)
COPD	1.29 (0.65-2.59)	$P = 0.28$ (NS)
Connective tishue disease	1.23 (0.51-2.96)	$P = 0.25$ (NS)
Carcinoma without metastases	0.73 (0.26-2.06)	$P = 0.37$ (NS)
Bronchial asthma	0.42 (0.13-1.38)	$P = 0.98$ (NS)

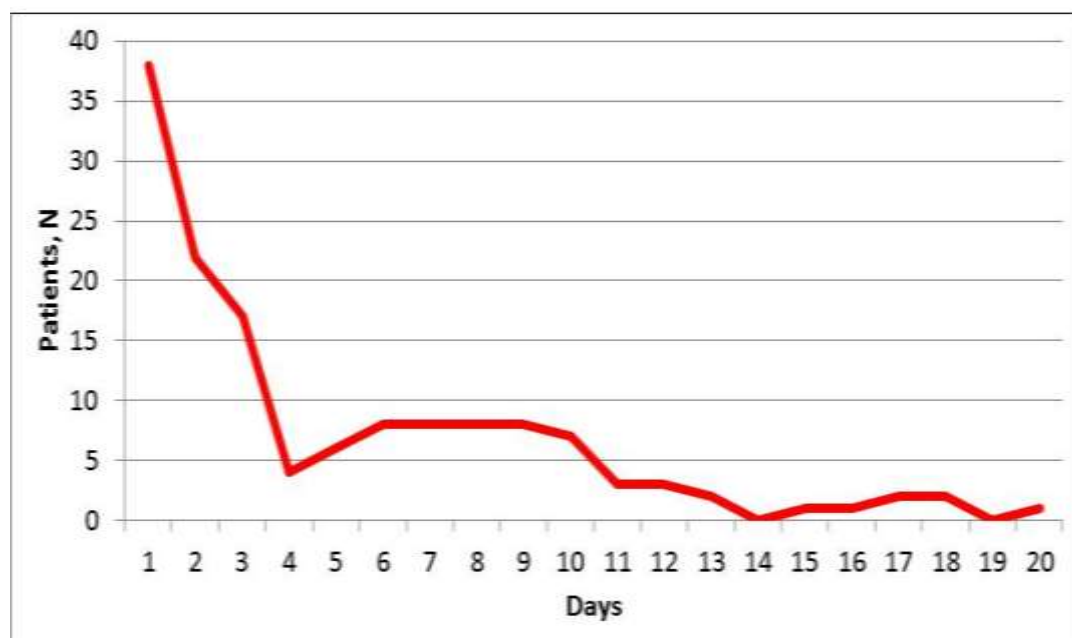
The most common complication of pneumonia among the deceased patients was acute respiratory failure –133 patients ( 89.9%); 33 patients (22.3%) of the cases required intubation and mechanical ventilation. Pleural effusion had 48 patients (32.4% of the deceased). Hypotension requiring inotropic support had 71 patients (48%). The most common extrapulmonary complication was acute renal failure (40 patients- 27%), followed by the acute gastrointestinal bleeding (15 patients – 10.1%).

We determined the severity of pneumonia of the deceased patients according to the three main scales - IDSA/ATS criteria, PSI and CURB-65. According to the IDSA/ATS criteria, 16.9% of the deceased were classified as non-severe pneumonia at the time of hospitalization. According to the PSI 9.5% of the deceased fell into the low risk groups, and according to CURB-65 13.9% of the deceased were classified as low-risk patients and 15.3% of the deceased had an intermediate risk (Fig.2)



**Figure 2: Distribution of the deceased patients according to different severity scales**

We examined the time from hospitalization to death, and found that the highest mortality rate was observed in the first three days of hospitalization then it dropped considerably. Most of the deceased patients (52%) died within the first 3 days of the hospital stay (Fig 3).



**Figure 3: Length of stay of the deceased patients**

## DISCUSSION

The mortality rate in our clinic corresponds to that in literature, slightly higher than this in Europe (9.1%) and the USA/Canada (7.3%) and lower than this in Latin America (13.3%)<sup>7</sup>. Mortality in different European countries also varies widely, according to various authors - in Switzerland it is 8%<sup>8</sup> and in France – 16.3%<sup>9</sup>. Most likely, the wide variation in mortality according to different studies is due to a different design of the studies. For ICU we found a high mortality rate (45.7%), which is not surprising considering that there were treated the most severe pneumonia cases with many complications. Other authors also report similar mortality rate in ICU. Paganin established mortality in ICU in France 43%<sup>10</sup>. We found a low



percentage of intubated and mechanically ventilated patients (22.3%). A similar percentage of intubated patients was found also by Ewig<sup>11</sup>. The low percentage of intubated patients is due to the elderly patients and those with severe chronic irreversible diseases, which limit the therapeutic options. Looking at the mortality rates in different age groups, we found the lowest rate in the 31-40 years group, then it started gradually to increase and in the age over 80 years it reached up to 20.9%. The mortality rate of 5.1% in the youngest age group under 30 years was most likely related to the fact that several patients with concomitant severe pathology, such as childhood cerebral palsy, cystic fibrosis and others fell into this group. Almost all authors establish mortality increase with age, as do our results<sup>12, 13, 14</sup>. It is not coincidental that age is a risk criterion in both the major severity scales CURB-65 and PSI. Some critics of the severity scales even believe that in PSI, age is overstated as a risk factor, whereas the severity of pneumonia in young patients may remain underestimated.

The risk of mortality increases with the presence of comorbidities. We found that the highest mortality risk had patients with dementia, carcinoma with metastases and cerebrovascular disease. Similar results were reported by other authors. Kaplan et al. found malignancy (OR - 2.26 95% CI 2.2-2.33), renal disease (OR 2.15 95% CI 1.95-2.25), liver disease (OR 2.1, 95% CI 1, 87-2.34), myocardial infarction (OR 1.53 95% CI 1.47-1.59) and congestive heart failure (OR 1.53 95% CI 1.47-1.59) as predictors of increased mortality<sup>12</sup>. Ewig found the highest mortality in the group of malignancies (including non-lung and lung carcinomas, 28.2% and 25.2% respectively), pulmonary diseases other than COPD (24.4%) and dementia (22.3%)<sup>11</sup>. In our study dementia carried the highest risk of death. Wesemann also found that hemiplegia, dementia, and chronic heart failure were significantly associated with one-year mortality, with CCI and CURB-65 having a similar predictive value<sup>15</sup>. The CCI is the most widely used scale to assess the cumulative burden of concomitant diseases on the outcome of a particular disease. The index was published in 1987 by M. Charlson et al.<sup>16</sup>. We found significantly higher CCI in deceased patients compared to survivors, as reported by Pereira<sup>17</sup> and Cabrera<sup>18</sup>. We believe that determining the CCI in patients with CAP may contribute to the identification of high risk patients. CRP is the most widely used marker of inflammation in CAP. We found that it was significantly higher in deceased patients, which could be associated with a more pronounced systemic inflammatory response. The results about CRP as a predictor of mortality are controversial. Some authors also found significantly higher CRP in the deceased<sup>19, 20</sup> while others did not detect such correlation<sup>21</sup>. Severity scales are a major tool for determining the severity and risk of mortality. However, their results cannot be the only predictive criterion. We found deceased patients who were classified as low-risk for mortality according to the three scales CURB-65, PSI and IDSA/ATS criteria. This indicates

that pneumonia may be a progressive disease, and patients who are considered as stable and low risk for death may dramatically deteriorate. The highest mortality rate was found in the first 3 days of hospitalization. This suggests that all patients with CAP should be managed with caution in the first 3 days, even if they are classified as low-risk at the time of hospitalization. The possibility of a rapid deterioration in the clinical course of the disease requires close monitoring, especially in the first 3 days when the probability of developing complications and adverse outcome is the highest. Naturally particular caution need patients with an increased risk of mortality assessed by the main scales. Authors like Ewig and Torres even compare severe pneumonia with acute myocardial infarction and offer just as urgent measures when treating these patients<sup>22</sup>. Kolditz also offers intensified monitoring in patients with severe CAP<sup>23</sup>. Such an approach would, also in our view, contribute to reducing CAP mortality, and again we want to emphasize the need of active monitoring not only of high-risk but also of low-risk patients with CAP because of the dynamic and potentially adverse course of the disease.

## CONCLUSION:

Older patients with comorbidities had higher risk of dying in the hospital. Patients with CAP need intensified monitoring especially in the first 3 days even if they do not have severe pneumonia on admission.

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