Acta Medica 2023; 54(1): 71-79 DOI: 10.32552/2023.ActaMedica.887

acta medica

ORIGINAL ARTICLE

Evaluating the Correlation of Mortality and Biochemical Parameters in Community-acquired and Hospital-acquired Pneumonia

Başak Çeltikçi[1]
ORCID: 0000-0002-3242-978X

Esen Sayın Gülensoy[2]
ORCID: 0000-0002-0154-7775

[1] Hacettepe University, Faculty of Medicine, Department of Biochemistry, Ankara, Türkiye.

[2] Ufuk University, Faculty of Medicine, Department of Chest Diseases, Ankara, Türkiye.

Corresponding Author: Başak Çeltikçi
E-mail: basakceltics@gmail.com

Received: 8 March 2023, Accepted: 24 March 2023,
Published online: 31 March 2023

ABSTRACT

Objective: The associations of inflammation and immunity of host lead to higher mortality in both community-acquired and hospital-acquired pneumonia patients. Therefore, several inflammatory and immunological biomarkers are essential for diagnosis, prognosis, and survival. Among these inflammatory markers, such as older age, and higher blood urea nitrogen, creatinine, procalcitonin and C-reactive protein, and lower albumin levels have been shown to have strong correlations with worse outcomes and high mortality, especially in community-acquired pneumonia patients. In this study, we investigated the correlation between several biochemical markers, which are mostly involved in inflammation, and mortality in not only community-acquired but also hospital-acquired pneumonia patients.

Material and Methods: This was a retrospective study of hospitalized community-acquired and hospital-acquired pneumonia patients in a third degree university hospital. In their initial blood tests (also used for diagnosis), blood urea nitrogen, creatinine, procalcitonin, C-reactive protein and albumin levels, and white blood cell, lymphocyte, neutrophil, platelet and erythrocyte counts, red blood cell distribution width and hemoglobin levels were measured. The outcome variable was mortality at 30 days. Statistical analysis included univariate comparisons of continuous variables between deceased and survivor groups, subject to mortality analysis and logistic regression in both community-acquired and hospital-acquired pneumonia patients.

Results: 272 hospitalized community-acquired and 80 hospital-acquired pneumonia patients were included. Patients who died during follow-up had older age and higher levels of procalcitonin, blood urea nitrogen, creatinine, and red blood cell distribution width in community-acquired pneumonia group. Remarkably, logistic regression analysis showed a significant relationship between creatinine and mortality, regardless of age, severity of community-acquired pneumonia and comorbidities. Creatinine is a strong independent prognostic factor, subject to mortality in community-acquired pneumonia group.

Conclusions: Older age, higher procalcitonin, blood urea nitrogen, creatinine and red blood cell distribution width levels are significant biomarkers for prediction of higher mortality in hospitalized community-acquired pneumonia patients.

Keywords: community-acquired pneumonia, hospital-acquired pneumonia, mortality, creatinine.

INTRODUCTION

Pneumonia is a common infectious disease that causes inflammation in the lung tissue and a major cause of mortality among infectious diseases globally. It is usually caused by various bacteria, viruses, and other microorganisms, and can lead to severe respiratory distress, hospitalization, and mortality. Mortality rates in pneumonia vary significantly based on the type of pneumonia, patient demographics, and pre-existing medical conditions, such as hypertension, diabetes mellitus, immune deficiencies, chronic kidney diseases or chronic obstructive pulmonary diseases [1]. Clinical scores, such as CURB-65 (confusion, urea, respiratory, blood pressure, >65 years)/ CRB-65 (confusion, respiratory, blood pressure) and pneumonia severity index (PSI) are used for indication of hospitalization, presence of severe complications and assessment of mortality. However, these scales have certain limitations, such as confusion assessment error, time consuming and expensive [2, 3]. Therefore, several biochemical (inflammatory and immunological) parameters have been studied in the context of community-acquired and hospital-acquired pneumonias, with the aim of identifying predictors of mortality and prognosis for improving patient outcomes [2, 4]. In this study, we aimed to serve additional evidence to the current literature on the effect of biochemical parameters on mortality in patients having community-acquired and hospital-acquired pneumonias.

Community-acquired Pneumonia (CAP)

CAP, the leading cause of death from infectious diseases worldwide, is a type of pneumonia that develops outside the hospital setting. It is a common respiratory illness and can lead to severe morbidity and mortality, especially in elderly patients or those with underlying health conditions. Various biochemical parameters have been studied in CAP, with the aim of identifying predictors of prognosis and mortality [2, 4] [3, 5].

C-reactive protein (CRP) is a biomarker of inflammation and is produced by the liver, in response to infections. CRP is elevated in bacterial as well as viral infections. Several studies have evaluated the role of CRP in predicting mortality in CAP. A study by Kruger et al. found that elevated levels of CRP (>150 mg/L) were associated with an increased risk of mortality in CAP patients [6]. Similarly, a study by Coelho et al. found that CRP levels were significantly higher in non-survivors of CAP, compared to survivors [7].

Procalcitonin (PCT) is another biomarker of infection that has been studied in the context of CAP. PCT is produced by various tissues and cells, including the thyroid gland and lungs, in response to bacterial infections. Since PCT is a blood marker for bacterial infections, PCT-guided therapy has proven to allow a significant reduction of duration and frequency of antibiotic therapy. A meta-analysis by Schuetz et al. found that PCT was a reliable predictor of mortality in CAP, with higher PCT levels being associated with increased mortality [8]. However, another study by Kutz et al. found that PCT levels were not significantly associated with mortality in CAP patients. In primary care and intensive care unit patients, no significant association of initial PCT levels and outcome was found [9].

Albumin is a protein synthesized by the liver and is involved in various physiological functions, including the regulation of osmotic pressure and the transport of various substances in the blood. Several studies have evaluated the role of albumin levels in predicting mortality in CAP. A study by Arnau-Barrés et al. found that low albumin levels were associated with increased mortality in CAP patients [10]. Similarly, a study by Eshwara et al. found that low albumin levels were an independent predictor of mortality in CAP patients [11]. Low albumin levels, ICU transfer and development of CAP-associated complications were found to be additional independent risk factors for prolonged length of hospital stay [12].

Additional biomarkers, such as prealbumin, Neutrophil Count Percentage (NCP) and Neutrophil/ Lymphocyte Ratio (NLR), pro-adrenomedullin (proADM) and pro-atrial natriuretic peptide (proANP), have been studied for predicting mortality in CAP. Serum Prealbumin Improves the Sensitivity of Pneumonia Severity Index in Predicting 30-day Mortality of CAP Patients [13]. NCP and NLR are promising candidate predictors of mortality for hospitalized CAP patients [5]. NLR improves the accuracy of PSI in predicting 30-day mortality of CAP patients [14]. NLR in adult CAP patients correlates with unfavorable clinical outcomes [15]. In addition, proADM and proANP accurately predict short- and long-term all-cause mortality, prognosis and survival in CAP patients [16, 17].

Hospital-acquired Pneumonia (HAP)

Hospital-acquired pneumonia (HAP) is a type of pneumonia that develops in patients who are hospitalized for other medical conditions. It usually develops 48 hours after hospitalization and is not known to be in the incubation period at admission and defined as a pneumonia that occurs within 48 hours of hospital discharge. HAP is associated with significant morbidity and mortality, and is often caused by multi-drug-resistant organisms. Various biochemical parameters have been studied in HAP, with the aim of identifying predictors of mortality.

Procalcitonin (PCT) has been studied in the context of HAP, with the aim of differentiating between bacterial and non-bacterial causes of HAP. A meta-analysis by Liu et al. found that PCT was a reliable biomarker for differentiating between bacterial and non-bacterial causes of HAP, with higher PCT levels being associated with a higher likelihood of bacterial HAP [18]. However, the role of PCT in predicting mortality in HAP is less clear. A study by Yilmaz et al. found that PCT levels were not significantly associated with mortality in HAP patients [19].

MATERIALS AND METHODS

Patient evaluation

Inclusion criteria for our study were being above 18 years old and diagnosed with either CAP or HAP. Patients were grouped, according to diagnostic criteria for CAP and HAP in ATS/IDSA guidelines.

The diagnosis of CAP generally requires the demonstration of an opacity on chest imaging in a patient with a clinically compatible syndrome (eg, fever, dyspnea, cough, and sputum production), leukocytosis and elevations in creatinine and BUN levels [20].

HAP were diagnosed if two or more of the following clinical features are present: temperature greater than 38°C or less than 36°C; leukopenia or leukocytosis; purulent tracheal secretions and decreased partial pressure of oxygen in arterial blood [21].

Exclusion criteria for our study were being below 18 years old, pregnancy, having active infection except pneumonia, chronic kidney diseases, malignancies, connective tissue diseases and immunosuppressive treatment in a month.

In our study, patients were categorized, according to their gender, age, 30-day mortality (deceased or survivor), pneumonia type (community-acquired pneumonia vs hospital-acquired pneumonia), pneumonia evaluation score (for community-acquired pneumonia only) (CURB-65), cardiac additional disease (congestive heart failure and hypertension/coronary artery disease), neurological additional disease, and co-morbidities as COPD and DM.

This was a retrospective study of hospitalized CAP and HAP patients in a third degree university hospital. 272 community-acquired pneumonia patients and 80 hospital-acquired pneumonia patients who were followed up in the inpatient service in between January 2012 and December 2018 were included in the study, with the ethical approval of Ufuk University Ethical Committee (Approval No:12024861-10/12.01.2023). The 30-day mortality of the patients from the day of admission to the hospital were recorded. The patients were divided into two groups, according to their survival or death status.

In their initial blood tests which were obtained at admission, following parameters were studied: WBC numeric value (normal range 4.6-10.2 x103/µL), Hb (normal range 11.7-17 g/dL), RDW (10-17.6% normal range: under and above 15%), CRP value (normal range 0-0.5 mg/dL), PCT value (<0.5 ng/mL low risk, >2 ng/mL high risk), platelet value (normal range 142-450x10 3/µL), albumin value (normal range 3-5 mg/dL), BUN value (normal range 8-23 mg/dL), creatinine value (normal range 0.5-1.2 mg/dL). Location of abnormalities in chest x-ray (lobar vs multilobar) and specific chest x-ray radiological examination (consolidation, ground glass or consolidation and ground glass) were examined. All these parameters were evaluated in these patients having community-acquired or hospital-acquired pneumonia.

WBC counts were measured by fluorescent flow scatter. Hb was measured by sodium lauryl sulfate precipitation, RDW and platelet counts were measured by electric impedance.

Serum CRP levels were measured by nephelometric/turbidometric method (Beckman).

Serum PCT levels were measured by chemiluminescent magnetic particle separation assay (Beckman).

Serum albumin levels were measured by bromocresol based assay (Beckman).

Serum BUN levels were measured by an enzymatic (urease) method (Beckman).

Serum creatinine levels were measured by alkaline picrate based assay (Beckman).

Statistics

SPSS and R software were used for statistical analysis. The significance threshold was accepted as $p \leq 0.05$. Depending on parametric assumptions, continuous variables were given as mean ± SD or median as 1st and 3rd quartiles (descriptive statistics). Discontinuous variables were given as absolute frequency (n) and relative frequency (%). Univariate comparisons of continuous variables between groups subject to mortality analysis were performed with appropriate parametric or non-parametric tests (Student's t-test, Mann-Whitney U). When it was necessary to look at the correlations, the Spearman or Pearson correlation coefficients were used again according to whether the parametric assumptions are met or not. Simple logistic regression or Cox regression analyzes was performed to identify parameters that have independent effects on mortality (depending on assumptions and univariate results).

RESULTS

Demographic characteristics, comorbidities and laboratory test results were compared (Table 1, 2 and 3). The seven statistically significant results in univariate analysis (95% confidence interval) were: Age (mean 81.5 years old vs 72 years old, $p < 0.001$), CURB-65 score (mean 4 vs 3, $p < 0.001$), RDW (17.3% vs 16.05%, $p = 0.017$), CRP (73.1 mg/L vs 26.23 mg/L, $p=0.047$), PCT (1.51 ng/mL vs 0.44 ng/mL, $p=0.038$), BUN (47 mg/dL vs 26 mg/dL, $p < 0.001$) and creatinine (1.67 mg/dL vs 1 mg/dL, $p < 0.001$) in CAP cases with respect to mortality (Table 1).

Older age, high RDW and creatinine levels were significantly correlated with mortality in CAP in logistic regression analysis, respectively $p<0.001$, OR=1.078; $p=0.024$, OR=1.114; $p<0.001$, OR=1.691 (Table 2). Creatinine was found to be a very strong factor (Table 2). There was no statistical difference in univariate analysis of hospital-acquired pneumonia (Table 3).

DISCUSSION

Since, despite recent advances in antimicrobial treatment, CAP is still the leading cause of death from infectious diseases worldwide, the discovery of novel diagnostic and prognostic biomarkers, showing the expression of the host's inflammatory response against the pathogen microorganism, and host's immunity is essential for improving patient management in CAP. CRP, PCT, and several inflammatory cytokines, such as Interleukins (IL) IL-1 and 6 are the most frequently studied [2, 16].

In addition, HAP is also associated with significant morbidity and mortality, and is often caused by multi-drug-resistant organisms. Similarly, several diagnostic and prognostic biomarkers, such as PCT is studied in several studies to improve patient outcome and evaluate the risk of mortality [18].

CURB (confusion, uremia, abnormal respiratory rate and low blood pressure) is used to identify patients with CAP who may be candidates for outpatient vs. inpatient treatment. Because of the limitations in clinical scores, such as CURB or PSI, several studies evaluated the predictive role of various inflammatory and immunological biomarkers for predicting mortality and prognosis in pneumonia patients.

PCT can help guide the decision to initiate or discontinue antibiotic treatment in patients with established diagnoses of CAP [22]. Even though PCT is a good marker for the assessment of severity and mortality of CAP patients [23, 24], the combination of PCT and CURB-65 was more accurate than other prognostic models in predicting mortality [25]. Both IL-6 and PCT are significant for prediction of 30-day mortality in hospitalized patients with CAP [26]. PCT levels were positively correlated with PSI and CURB-65 scores [27]. In another study, PCT was not an independent predictor of 30-day mortality and its increased levels were correlated with pneumonia severity, but not CRP levels [28].

Table 1. Summary of community-acquired pneumonia cases with respect to mortality

	Deceased (n=48)	Survivors (n=224)	*p* value
Sex			
Male	29 (60.4%)	142 (63.4%)	0.699
Female	19 (39.6%)	82 (36.6%)	
Age (years, median (min-max))	81.5 (76-86)	72 (60-81)	**<0.001**
CURB-65 score	4 (3.5-4)	3 (3-3)	**<0.001**
Any comorbidity	35 (72.9%)	147 (65.6%)	0.330
Chronic heart failure	16 (33.3%)	53 (23.7%)	0.224
Hypertension or coronary artery disease	15 (31.3%)	73 (32.7%)	0.842
Any neurological comorbidity	6 (12.5%)	18 (8%)	0.478
Chronic obstructive pulmonary disease	12 (25%)	65 (29%)	0.575
Diabetes mellitus	6 (12.5%)	23 (10.3%)	0.844
White blood cell count (mm^3, median (min-max))	10.86 (7.8-16.2)	12.25 (8.17-16.09)	0.399
Low	6 (12.5%)	11 (4.9%)	
Normal	16 (33.3%)	78 (34.8%)	0.141
High	26 (54.2%)	135 (60.3%)	
Hemoglobin (g/dL, median (min-max))	13 (11-14)	12.65 (10.85-14)	0.514
Low	16 (33.3%)	86 (38.4%)	
Normal	29 (60.4%)	129 (57.6%)	0.680
High	3 (6.3%)	9 (4%)	
Red blood cell distribution width (%, median (min-max))	17.3 (15.35-18.9)	16.05 (14.05-18.3)	**0.017**
Low	0 (0%)	15 (6.7%)	
Normal	24 (50%)	129 (57.6%)	0.057
High	24 (50%)	80 (35.7%)	
<15	9 (18.8%)	83 (37.1%)	**0.015**
≥15	39 (81.3%)	141 (62.9%)	
C-reactive protein (mg/L, median (min-max))	73.1 (17.76-133.06)	26.23 (9.82-100.5)	0.047
Low	0 (0%)	0 (0%)	
Normal	7 (14.6%)	47 (21%)	0.313
High	41 (85.4%)	177 (79%)	
Procalcitonin (ng/mL, median (min-max))	1.51 (0.12-16.71)	0.44 (0.14-2.58)	**0.038**
Low	15 (31.3%)	95 (42.4%)	
Normal	11 (22.9%)	52 (23.2%)	0.266
High	22 (45.8%)	77 (34.4%)	
Platelet count (mm^3, median (min-max))	250 (164.5-327.5)	220 (162.5-295)	0.294
Low	10 (20.8%)	43 (19.2%)	
Normal	34 (70.8%)	160 (71.4%)	0.950
High	4 (8.3%)	21 (9.4%)	
Albumin (mg/dL, median (min-max))	2.75 (2.3-3.35)	2.9 (2.6-3.3)	0.127
Low	29 (60.4%)	122 (54.5%)	
Normal	19 (39.6%)	101 (45.1%)	0.691
High	0 (0%)	1 (0.4%)	
Urea (mg/dL, median (min-max))	47 (24.5-73.5)	26 (15-52.5)	**<0.001**
Low	0 (0%)	0 (0%)	
Normal	14 (29.2%)	118 (52.7%)	0.003
High	34 (70.8%)	106 (47.3%)	
Creatinine (mg/dL, median (min-max))	1.67 (1.19-2.34)	1 (0.7-1.38)	**<0.001**
Low	0 (0%)	26 (11.6%)	
Normal	12 (25%)	113 (50.4%)	**<0.001**
High	36 (75%)	85 (37.9%)	
Pulmonary involvement			
Lobar	26 (54.2%)	127 (56.7%)	0.748
Multilobar	22 (45.8%)	97 (43.3%)	
X-ray findings			
Consolidation	19 (39.6%)	126 (56.3%)	
Ground-glass opacity	14 (29.2%)	55 (24.6%)	0.079
Both	15 (31.3%)	43 (19.2%)	

Table 2. Parameters independently associated with mortality in patients with community-acquired pneumonia

	Beta coef.	Std. Error	Wald	p value	OR	95% CI for OR	
Age	0.075	0.018	18.304	**<0.001**	**1.078**	1.042	1.116
RDW	0.108	0.048	5.115	**0.024**	**1.114**	1.014	1.223
Creatinine	0.525	0.151	12.113	**0.001**	**1.691**	1.258	2.273
Constant	-9.875	1.763	31.383	<0.001	0	–	–

OR: odds ratio, CI: confidence interval, RDW: red blood cell distribution width.

Final step (#3) of the backward stepwise method is shown. Variables included in the model (step #1): Age, RDW, procalcitonin, urea, creatinine.

Hosmer and Lemeshow statistic: 0.979, Nagelkerke R2: 0.249.

In addition, CRP and PCT support the diagnosis of pneumonia and help distinguish bacterial from viral causes of CAP, but studies have found that these tests reliably add no value to the initial clinical and radiographic evaluation [29]. The reported sensitivity and specificity of CRP for pneumonia both range from approximately 40 to 90 percent and vary substantially with the cutoff value used [30-36]. Similarly, the reported sensitivity for procalcitonin ranges widely from 38 to 91 percent [20]. Elevated CRP values cannot support a diagnosis of bacterial infection when the illness has lasted less than 7 days, but may indicate a complication of viral infection after a week [37].

Overall, CRP, WBC counts and ILs are non-specific for diagnosing pneumonia, besides PCT may not be effective to distinguish between bacterial versus viral infections, only can used for monitoring response to antimicrobial therapy. Additionally, increased procalcitonin concentrations were shown following surgery, trauma, and in systemic viral infections [22].

Among these biochemical markers, as we described in details in the introduction, elevated serum creatinine level was reported as an independent predictor of in–hospital mortality in severe CAP patients [38], similar to our study. This study created a novel clinical model named CLCGH scoring system, including serum creatinine>259.5μmol/L, WBC>17.35×109/L, CRP>189.4μg/mL, Glasgow Coma Scale ≤9 and serum bicarbonate ≤17.65mmol/L and each index was an independent factor for hospital mortality in severe CAP [38]. In another study, serum creatinine levels above the 1.1 mg/dL and blood urea nitrogen levels above 21 mg/dL were associated with an increased risk of mortality in univariate analysis [39]. Similar to our study, Sloane et al. reported that 20% rise in serum creatinine level above baseline was associated with 30–days mortality in CAP patients [3, 40].

Besides, in a recent study, arrival serum markers, such as BUN, albumin, creatinine, BUN/albumin ratio and BUN/creatinine ratio, were correlated with the incidence of mortality during hospitalization. When survivors and non-survivors were compared, creatinine >/= 2.8 mg/dL showed the highest odds (OR = 7.656, 95% CI = 2.281-25.692; p = 0.001); followed by CURB-65 score >/= 4 (OR = 4.958, 95% CI = 0.418-58.784; p = 0.266); and BUN >/= 24.7 mg/dL (OR = 3.364, 95% CI = 1.033-10.954; p = 0.062). Similar to our study, serum creatinine was a fair predictor of in-hospital mortality (AUC = 0.721) showed 53.0% sensitivity and 87.0% specificity at cut-off 2.8 mg/dL. Among five serum markers, increased serum creatinine was a better predictor of in-hospital mortality in adults having CAP [3].

As it is known, using creatinine as a biomarker in CAP patients is limited due to the comorbidities, such as chronic kidney disease, which we excluded in our study. Initial increased creatinine (>1.5 mg/dL) levels were found to be not a risk factor for early mortality, but a risk factor for pulmonary complications, so alterations in renal function tests should be evaluated [41].

In our study, we found that in addition to older age, higher CURB-65 score, BUN, creatinine, RDW, CRP and PCT levels were statistically significant in CAP cases, with respect to mortality (Table 1). Similar to the study of Adnan et al, serum creatinine levels were an independent strongest predictor of mortality in CAP patients (Table 2). Creatinine was found to be a very strong factor (Table 2), but it is important to keep in mind that creatinine is a parameter that acts in a very narrow range and easily differs, because of the comorbidities.

We could not find any significant difference between survivors and deceased in HAP patients. Similar to our study, Yilmaz et al. could not find any significant biomarkers in HAP patients [19]. We have 80 HAP patients in our study, compared to 272

Table 3. Summary of hospital-acquired pneumonia cases with respect to mortality

	Deceased (n=17)	Survivors (n=63)	*p value*
Sex			
Male	11 (64.7%)	41 (65.1%)	1.000
Female	6 (35.3%)	22 (34.9%)	
Age (years, median (min-max))	80 (73-85)	75 (68-81)	0.111
Any comorbidity	14 (82.4%)	57 (90.5%)	0.611
Chronic heart failure	5 (29.4%)	24 (38.1%)	0.706
Hypertension or coronary artery disease	10 (58.8%)	33 (52.4%)	0.842
Any neurological comorbidity	6 (35.3%)	17 (27%)	0.711
Chronic obstructive pulmonary disease	11 (64.7%)	46 (73%)	0.711
Diabetes mellitus	4 (23.5%)	13 (20.6%)	1.000
White blood cell count (mm^3, median (min-max))	12.9 (10.6-15.6)	14.7 (11.2-19.7)	0.108
Low	0 (0%)	0 (0%)	
Normal	4 (23.5%)	12 (19%)	0.682
High	13 (76.5%)	51 (81%)	
Hemoglobin (g/dL, median (min-max))	11.5 (10.5-12.8)	11.9 (9.81-14.1)	0.764
Low	10 (58.8%)	33 (52.4%)	
Normal	6 (35.3%)	25 (39.7%)	0.885
High	1 (5.9%)	5 (7.9%)	
Red blood cell distribution width (%, median (min-max))	17.9 (16.8-18.8)	18.2 (16.8-20.1)	0.414
Low	0 (0%)	0 (0%)	
Normal	7 (41.2%)	17 (27%)	0.257
High	10 (58.8%)	46 (73%)	
<15	1 (5.9%)	5 (7.9%)	1.000
≥15	16 (94.1%)	58 (92.1%)	
C-reactive protein (mg/L, median (min-max))	7.71 (4.54-16.52)	10.29 (5-18.8)	0.480
Low	0 (0%)	0 (0%)	
Normal	6 (35.3%)	18 (28.6%)	0.591
High	11 (64.7%)	45 (71.4%)	
Procalcitonin (ng/mL, median (min-max))	0.63 (0.27-4.9)	0.48 (0.24-2.31)	0.720
Low	6 (35.3%)	33 (52.4%)	
Normal	6 (35.3%)	16 (25.4%)	0.456
High	5 (29.4%)	14 (22.2%)	
Platelet count (mm^3, median (min-max))	220 (142-288)	220 (153-282)	0.906
Low	4 (23.5%)	12 (19%)	
Normal	12 (70.6%)	46 (73%)	0.896
High	1 (5.9%)	5 (7.9%)	
Albumin (mg/dL, median (min-max))	3.1 (2.8-3.2)	3 (2.7-3.6)	0.625
Low	6 (35.3%)	26 (41.3%)	
Normal	11 (64.7%)	37 (58.7%)	0.655
High	0 (0%)	0 (0%)	
Urea (mg/dL, median (min-max))	34 (20-52)	26 (19-37)	0.203
Low	0 (0%)	0 (0%)	
Normal	5 (29.4%)	28 (44.4%)	0.401
High	12 (70.6%)	35 (55.6%)	
Creatinine (mg/dL, median (min-max))	0.78 (0.64-1.12)	0.78 (0.65-1.04)	0.676
Low	0 (0%)	0 (0%)	
Normal	12 (70.6%)	52 (82.5%)	0.274
High	5 (29.4%)	11 (17.5%)	
Pulmonary involvement			
Lobar	10 (58.8%)	24 (38.1%)	0.208
Multilobar	7 (41.2%)	39 (61.9%)	
X-ray findings			
Consolidation	6 (35.3%)	18 (28.6%)	
Ground-glass opacity	3 (17.6%)	7 (11.1%)	0.586
Both	8 (47.1%)	38 (60.3%)	

CAP patients. The difference between survivors and deceased in HAP patients can be significant with a larger sample size.

We could not evaluate 90-day mortality in the survivor group, since most of the patients have been discharged from hospital before 90 days and unfortunately, we could not reach that information. With a larger sample size, we believe that we can evaluate 90-day mortality.

In this study, we aimed to serve additional evidence to the current literature on the effect of biochemical parameters on mortality in patients having CAP and HAP. Even though we found seven parameters strongly significant and in addition, creatinine as an independent strongest predictor of mortality in CAP patients, we believe that with a relatively larger patient size, we will get new biochemical biomarkers that are more significant in both CAP and HAP patients, with respect to mortality for patient management. We can use these biomarkers independently or with pneumonia severity assessment scales, in order to prevent the risk of complications and mortality, especially in CAP patients.

Author contribution

Study conception and design: ESG and BC; data collection: ESG and BC; analysis and interpretation of results: ESG and BC; draft manuscript preparation: BC. All authors reviewed the results and approved the final version of the manuscript.

Ethical approval

The study was approved by the Ufuk University Ethical Committee (Approval No:12024861-10/12.01.2023).

Funding

The authors declare that the study received no funding.

Conflict of interest

The authors declare that there is no conflict of interest.

REFERENCES

[1] Lanks, C.W., A.I. Musani, and D.W. Hsia, Community-acquired Pneumonia and Hospital-acquired Pneumonia. Med Clin North Am, 2019. 103(3): p. 487-501.

[2] Torres, A., et al., Biomarkers and community-acquired pneumonia: tailoring management with biological data. Semin Respir Crit Care Med, 2012. 33(3): p. 266-71.

[3] Adnan, M., et al., Prognostic value of five serum markers predicting in-hospital mortality among adults with community acquired pneumonia. J Infect Dev Ctries, 2022. 16(1): p. 166-172.

[4] Kutz, A., et al., Pre-analytic factors and initial biomarker levels in community-acquired pneumonia patients. BMC Anesthesiol, 2014. 14: p. 102.

[5] Curbelo, J., et al., Inflammation biomarkers in blood as mortality predictors in community-acquired pneumonia admitted patients: Importance of comparison with neutrophil count percentage or neutrophil-lymphocyte ratio. PLoS One, 2017. 12(3): p. e0173947.

[6] Kruger, S. and T. Welte, Biomarkers in community-acquired pneumonia. Expert Rev Respir Med, 2012. 6(2): p. 203-14.

[7] Coelho, L.M., et al., Patterns of c-reactive protein RATIO response in severe community-acquired pneumonia: a cohort study. Crit Care, 2012. 16(2): p. R53.

[8] Schuetz, P., et al., Procalcitonin to initiate or discontinue antibiotics in acute respiratory tract infections. Cochrane Database Syst Rev, 2017. 10(10): p. CD007498.

[9] Kutz, A., et al., Prognostic value of procalcitonin in respiratory tract infections across clinical settings. Crit Care, 2015. 19(1): p. 74.

[10] Arnau-Barres, I., et al., Serum albumin is a strong predictor of sepsis outcome in elderly patients. Eur J Clin Microbiol Infect Dis, 2019. 38(4): p. 743-746.

[11] Eshwara, V.K., C. Mukhopadhyay, and J. Rello, Community-acquired bacterial pneumonia in adults: An update. Indian J Med Res, 2020. 151(4): p. 287-302.

[12] Suter-Widmer, I., et al., Predictors for length of hospital stay in patients with community-acquired pneumonia: results from a Swiss multicenter study. BMC Pulm Med, 2012. 12: p. 21.

[13] Zhang, H.F., et al., Serum Prealbumin Improves the Sensitivity of Pneumonia Severity Index in Predicting 30-day Mortality of CAP Patients. Clin Lab, 2020. 66(5).

[14] Zhang, H.F., et al., Neutrophil-to-Lymphocyte Ratio Improves the Accuracy and Sensitivity of Pneumonia Severity Index in Predicting 30-Day Mortality of CAP Patients. Clin Lab, 2019. 65(10).

[15] Ge, Y.L., et al., Neutrophil-to-Lymphocyte Ratio in Adult Community-Acquired Pneumonia Patients Correlates with Unfavorable Clinical Outcomes. Clin Lab, 2019. 65(5).

[16] Nickler, M., et al., Prospective evaluation of biomarkers for prediction of quality of life in community-acquired pneumonia. Clin Chem Lab Med, 2016. 54(11): p. 1831-1846.

[17] Renaud, B., et al., Proadrenomedullin improves Risk of Early Admission to ICU score for predicting early severe community-acquired pneumonia. Chest, 2012. 142(6): p. 1447-1454.

[18] Liu, D., et al., Prognostic value of procalcitonin in pneumonia: A systematic review and meta-analysis. Respirology, 2016. 21(2): p. 280-8.

[19] Yilmaz, G., et al., Individualized antibiotic therapy in patients with ventilator-associated pneumonia. J Med Microbiol, 2017. 66(1): p. 78-82.

[20] Metlay, J.P., et al., Diagnosis and Treatment of Adults with Community-acquired Pneumonia. An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America. Am J Respir Crit Care Med, 2019. 200(7): p. e45-e67.

[21] Rotstein, C., et al., Clinical practice guidelines for hospital-acquired pneumonia and ventilator-associated pneumonia in adults. Can J Infect Dis Med Microbiol, 2008. 19(1): p. 19-53.

[22] Vijayan, A.L., et al., Procalcitonin: a promising diagnostic marker for sepsis and antibiotic therapy. J Intensive Care, 2017. 5: p. 51.

[23] Rumende, C.M. and D. Mahdi, Role of combined procalcitonin and lipopolysaccharide-binding protein as prognostic markers of mortality in patients with ventilator-associated pneumonia. Acta Med Indones, 2013. 45(2): p. 89-93.

[24] Pilotto, A., et al., Combined use of the multidimensional prognostic index (MPI) and procalcitonin serum levels in predicting 1-month mortality risk in older patients hospitalized with community-acquired pneumonia (CAP): a prospective study. Aging Clin Exp Res, 2018. 30(2): p. 193-197.

[25] Song, Y., et al., Prediction value of procalcitonin combining CURB-65 for 90-day mortality in community-acquired pneumonia. Expert Rev Respir Med, 2021. 15(5): p. 689-696.

[26] Andrijevic, I., et al., Interleukin-6 and procalcitonin as biomarkers in mortality prediction of hospitalized patients with community acquired pneumonia. Ann Thorac Med, 2014. 9(3): p. 162-7.

[27] Kasamatsu, Y., et al., Usefulness of a semi-quantitative procalcitonin test and the A-DROP Japanese prognostic scale for predicting mortality among adults hospitalized with community-acquired pneumonia. Respirology, 2012. 17(2): p. 330-6.

[28] Akagi, T., et al., Procalcitonin is not an independent predictor of 30-day mortality, albeit predicts pneumonia severity in patients with pneumonia acquired outside the hospital. BMC Geriatr, 2019. 19(1): p. 3.

[29] Huang, D.T., et al., Procalcitonin-Guided Use of Antibiotics for Lower Respiratory Tract Infection. N Engl J Med, 2018. 379(3): p. 236-249.

[30] Flanders, S.A., et al., Performance of a bedside C-reactive protein test in the diagnosis of community-acquired pneumonia in adults with acute cough. Am J Med, 2004. 116(8): p. 529-35.

[31] van Vugt, S.F., et al., Use of serum C reactive protein and procalcitonin concentrations in addition to symptoms and signs to predict pneumonia in patients presenting to primary care with acute cough: diagnostic study. BMJ, 2013. 346: p. f2450.

[32] Minnaard, M.C., et al., The added value of C-reactive protein measurement in diagnosing pneumonia in primary care: a meta-analysis of individual patient data. CMAJ, 2017. 189(2): p. E56-E63.

[33] Holm, A., et al., Aetiology and prediction of pneumonia in lower respiratory tract infection in primary care. Br J Gen Pract, 2007. 57(540): p. 547-54.

[34] Holm, A., et al., Procalcitonin versus C-reactive protein for predicting pneumonia in adults with lower respiratory tract infection in primary care. Br J Gen Pract, 2007. 57(540): p. 555-60.

[35] Almirall, J., et al., Contribution of C-reactive protein to the diagnosis and assessment of severity of community-acquired pneumonia. Chest, 2004. 125(4): p. 1335-42.

[36] Ruiz-Gonzalez, A., et al., The Diagnostic Value of Serum C-Reactive Protein for Identifying Pneumonia in Hospitalized Patients with Acute Respiratory Symptoms. J Biomark, 2016. 2016: p. 2198745.

[37] Melbye, H., et al., The course of C-reactive protein response in untreated upper respiratory tract infection. Br J Gen Pract, 2004. 54(506): p. 653-8.

[38] Wang, X., et al., A new method to predict hospital mortality in severe community acquired pneumonia. Eur J Intern Med, 2017. 40: p. 56-63.

[39] Celikhisar, H., G. Dasdemir Ilkhan, and C. Arabaci, Prognostic factors in elderly patients admitted to the intensive care unit with community-acquired pneumonia. Aging Male, 2020. 23(5): p. 1425-1431.

[40] Sloane, P.D., et al., The Nursing Home Pneumonia Risk Index: A Simple, Valid MDS-Based Method of Identifying 6-Month Risk for Pneumonia and Mortality. J Am Med Dir Assoc, 2017. 18(9): p. 810 e11-810 e14.

[41] Cilloniz, C., et al., Pulmonary complications of pneumococcal community-acquired pneumonia: incidence, predictors, and outcomes. Clin Microbiol Infect, 2012. 18(11): p. 1134-42.