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Correlation between Clinical Prognostic Factors and CAP Patients' Output due to Klebsiella Pneumoniae

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Abstract---Background: *Infections of K. Pneumoniae are often thought to be associated with higher mortality rates, this etiology has not been proven to be a clinical prognostic factor of death.*

Objectives*: to evaluate the relationship Between age, sex, delay of antibiotics administration, smoking status, hemoglobin, albumin, Chronic Obstructive Pulmonary Disease (COPD), diabetes mellitus (DM), cardiovascular disease, Patients Outcome Research Team (PORT) score, antibiotic resistance, Extended-spectrum β-lactamase (ESBL) strain through treatment length, (Intensive Care Unit) ICU admission indication, and mortality of community-acquired pneumonia (CAP) patients caused by K. Pneumoniae.*

Method*: The CAP patients infected with K. pneumoniae in the male and female pulmonology room of Dr. Soetomo General Hospital, Surabaya, Indonesia from 1 January 2009 to 31 December 2012 were analyzed in a retrospective cohort. Observed outcomes included treatment length, ICU admission indication, and mortality.*

Result*: The sample size fulfilling the inclusion was 41 patients. There was a significant correlation between comorbid COPD (10.000 OR, p = 0.018), DM (0.714 OR, p = 0.040), and PORT score (1.471 OR; p = 0.014) through ICU outpatient indications. In multivariate analysis, comorbid COPD (p = 0.013) was the most dominant independent factor through ICU indication care, whereas albumin (p = 0.040) and ESBL germs (p = 0.027) were the same dominant independent factors for mortality.*

Conclusion: *There was a relationship between comorbid COPD, DM, and PORT score on ICU indication care in univariate analysis.*

Keywords---*Community-Acquired Pneumonia, K. pneumoniae, clinical prognostic factors, infection*

I. Background

Epidemiology of community-acquired pneumonia (CAP) is not clear because few population-based statistics that are available. The Center for Disease Center (CDC) combines pneumonia with influenza when collecting morbidity and mortality data, although they do not combine it when collecting data in hospital[1]. Overall, the annual incidence of CAP has a range of 2 to 12 cases per 1000 people, with the highest incidence in infants and elderly[2,3]. Approximately

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10-20% of CAP patients require treatment in the intensive care unit (ICU), where 20-50% of them eventually passes away[4,5]. Streptococcus Pneumoniae is the most commonly identified pathogen in 20-60% of CAP cases in adults[2].

The last 5-year report from several pulmonary centers in Indonesia (Medan, Jakarta, Surabaya, Malang, Makassar) by taking different materials and methods of microbiological examination obtained sputum examination results as follows: 45.18% of Klebsiella Pneumoniae, 14.04% of Streptococcus pneumonia, 9.21% of Streptococcus viridans, 9% of Staphylococcus aureus, 8.56% of Pseudomonas aeruginosa, 7.89% of Streptococcus beta hemolytic, 5.26% of Enterobacter spp, 0.9% of Pseudomonas spp.[6]. In many Asian countries, K. Pneumoniae is the second most common pathogen responsible for CAP. Klebsiella pneumonia is gram-negative bacilli that is often involved in severe infection in community and nosocomial infections[7]. The germ has proven to be an independent risk factor for mortality in severe CAP[4]. Its distribution as a CAP pathogen is uneven worldwide with the highest incidence in developing countries and in Asia[8,9].

Klebsiella Pneumoniae is naturally resistant to amino penicillin (ampicillin or amoxicillin), an antibiotic commonly used as CAP first-line treatment in many developing countries. This has raised serious concerns since recent multicenter prospective studies in several Asian countries showed that K. Pneumoniae contributed for 15.4% of the pathogens responsible for hospital-treated CAP, after S. Pneumoniae. Furthermore, resistance appears among gram-negative bacilli such as extended spectrum β-lactamase (ESBL) thus increasingly recognized as a major public health problem in developed and developing countries[10,11].

In most published studies, the CAP etiology had not been identified as a risk factor of death. Although a specific CAP etiology, such as K. pneumoniae, is often suspected to be associated with higher mortality rates, this etiology has not been proven to be a prognostic factor of death[12]. Thus this kind of research is needed.

II. Method

The subjects of this study were CAP patients who were hospitalized in male and female ward of pulmonology Department at Dr. Soetomo General Hospital, Surabaya, Indonesia with K. pneumoniae sputum cultured treated from 1 January 2009 to 31 December 2012. The inclusion criteria were aged >18 years old, having one or more comorbids (COPD, DM, or KV) and with or without ESBL strains. Exclusion criteria were pulmonary tuberculosis, lungs malignant patients, kidney function disorder, liver disease, HIV; and sterile sputum cultures.

The data were collected from April to September 2013. Data obtained from the medical record were recorded and analyzed their association among age, sex, delay of antibiotics administration, smoking status, Hb, albumin, COPD, DM, KV, PORT score, antibiotic resistance, ESBL germs through hospitalized length, ICU admission indication, and mortality. Further analysis of related risk factors was performed using the SPSS (SPSS, Inc., Chicago, IL) with $p < 0.05$.

III. Result

The sample size was 41 CAP patients. Statistical analysis of each factor with indicated indications can be seen in tables 1, 2, 3. Assessing the fit model is to test the overall model whether the model produced is a fit model both before and after the independent variable is inserted into the model (table 4). When it was known that the regression model had fit with the data, coefficient value of determination logistic regression model from Nagelkerke's R Square value was examined (table 5). The coefficient values of each variable were in multiple logistic regression model, wald

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value and significant value. The significant value used as a reference to test the hypothesis. Wald and p values could be seen in table 6.

Table1: Correlation of prognostic factors and Indication of care in ICU

Variabel		ICU Indication		P	OR
		No	Yes		
Age					
< 65 years	Total (%)	25 (89.3)	3 (10.7)	0.084	5.208
≥ 65 years	Total (%)	8 (61.5)	5 (38.5)		
Sex					
Female	Total (%)	10 (100.0)	0 (0)	0.165	1.348
Male	Total (%)	23 (74.2)	8 (25.8)		
Smoking					
No	Total (%)	21 (91.3)	2 (8.7)	0.109	5.250
Yes	Total (%)	12 (66.7)	6 (33.3)		
COPD					
No	Total (%)	30 (88.2)	4 (11.8)	0.018	10.00
Yes	Total (%)	3 (42.9)	4 (57.1)		0
DM					
No	Total (%)	20 (71.4)	8 (28.6)	0.040	0.714
Yes	Total (%)	13 (100.0)	0 (0)		
Cardiovascular					
No	Total (%)	28 (82.4)	6 (17.6)	0.606	1.867
Yes	Total (%)	5 (71.4)	2 (28.6)		
Hb					
< 12	Total (%)	10 (100.0)	0 (0)	0.165	1.348
≥ 12	Total (%)	23 (74.2)	8 (25.8)		
Albumin					
< 3	Total (%)	8 (100)	0 (0)	0.318	1.320
≥ 3	Total (%)	25 (75.8)	8 (24.2)		
ESBL					
No	Total (%)	28 (82.4)	6 (17.6)	0.606	1.867
Yes	Total (%)	5 (71.4)	2 (28.6)		
Antibiotic resistent					
No	Total (%)	6 (85.7)	1 (14.3)	1.000	1.556
Yes	Total (%)	27 (79.4)	7 (20.6)		
Antibiotics admission length					
< 8 hours	Total (%)	22 (73.3)	8 (26.7)	0.083	0.733
≥ 8 hours	Total (%)	11 (100.0)	0 (0)		
PORT					
< 70	Total (%)	16 (100.0)	0 (0)	0.014	1.471
≥ 70	Total (%)	17 (68.0)	8 (32.0)		

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Table 2: Correlation between prognostic factors and mortality

Variable		Mortality		P	OR
		No	Yes		
Age					
< 65 years	Total (%)	24 (58.5)	4 (9.8)	1.000	1.091
≥ 65 years	Total (%)	11 (26.8)	2 (4.9)		
Sex					
Female	Total (%)	10 (24.4)	0 (0)	0.307	0.714
Male	Total (%)	25 (61.0)	6 (14.6)		
Smoking					
No	Total (%)	20 (48.8)	3 (7.3)	1.000	1.333
Yes	Total (%)	15 (36.6)	3 (7.3)		
COPD					
No	Total (%)	29 (70.7)	5 (12.2)	1.000	0.967
Yes	Total (%)	6 (14.6)	1 (2.4)		
DM					
No	Total (%)	25 (61.0)	3 (7.3)	0.361	2.500
Yes	Total (%)	10 (24.4)	3 (7.3)		
Cardiovascular					
No	Total (%)	30 (73.2)	4 (9.8)	0.268	3.000
Yes	Total (%)	5 (12.2)	2 (4.9)		
Hb					
< 12	Total (%)	9 (22.0)	1 (2.4)	1.000	1.731
≥ 12	Total (%)	26 (63.4)	5 (12.2)		
Albumin					
< 3	Total (%)	5 (12.2)	3 (7.3)	0.077	0.167
≥ 3	Total (%)	30 (73.2)	3 (7.3)		
ESBL					
No	Total (%)	31 (75.6)	3 (7.3)	0.051	7.750
Yes	Total (%)	4 (9.8)	3 (7.3)		
Antibiotic resistent					
No	Total (%)	7 (17.1)	0 (0.0)	0.567	0.800
Yes	Total (%)	28 (68.3)	6 (14.6)		
Antibiotics admission length					
< 8 hours	Total (%)	25 (61.0)	5 (12.2)	1.000	0.500
≥ 8 hours	Total (%)	10 (24.4)	1 (2.4)		
PORT					
< 70	Total (%)	15 (36.6)	1 (2.4)	0.376	3.750
≥ 70	Total (%)	20 (48.8)	5 (12.2)		

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Table 3: Correlation between prognostic factors and LOS

Variable		Mortality		P	OR
		No	Yes		
Age					
< 65 years	Total (%)	8 (19.5)	20 (48.8)	1.000	0.900
≥ 65 years	Total (%)	4 (9.8)	9 (22.0)		
Sex					
Female	Total (%)	5 (12.2)	5 (12.2)	0.124	3.429
Male	Total (%)	7 (17.1)	24 (58.5)		
Smoking					
No	Total (%)	7 (17.1)	16 (39.0)	1.000	1.138
Yes	Total (%)	5 (12.2)	3 (7.3)		
COPD					
No	Total (%)	10 (24.4)	24 (58.5)	1.000	1.042
Yes	Total (%)	6 (4.9)	1 (12.2)		
DM					
No	Total (%)	7 (17.1)	21 (51.2)	0.469	0.533
Yes	Total (%)	5 (12.2)	8 (19.5)		
Cardiovascular					
No	Total (%)	9 (22.0)	25 (61.0)	0.398	0.480
Yes	Total (%)	5 (7.3)	4 (9.8)		
Hb					
< 12	Total (%)	1 (2.4)	9 (22.0)	0.231	0.202
≥ 12	Total (%)	11 (26.8)	20 (48.8)		
Albumin					
< 3	Total (%)	1 (2.4)	7 (17.1)	0.398	0.286
≥ 3	Total (%)	11 (26.8)	22 (53.7)		
ESBL					
No	Total (%)	10 (24.4)	24 (58.5)	1.000	1.042
Yes	Total (%)	2 (4.9)	5 (12.2)		
Antibiotic resistent					
No	Total (%)	3 (7.3)	4 (9.8)	0.398	2.083
Yes	Total (%)	9 (22.0)	25 (61.0)		
Antibiotics admission length					
< 8 hours	Total (%)	10 (24.4)	20 (48.8)	0.457	2.250
≥ 8 hours	Total (%)	2 (4.9)	9 (22.0)		
PORT					
< 70	Total (%)	6 (14.6)	10 (24.4)	0.485	1.900
≥ 70	Total (%)	6 (14.6)	19 (46.3)		

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Table 4: Correlation among factors and rehospitalized incidence

Fit Model	-2 Log Likehood	
	Block number = 0	Block number = 1
ICU Indication	40.472	34.191
Mortality	34.137	24.870

Table 5. Determination coeficient

Fit Model	Nagelkerke's R Square
ICU Indication	0.226
Mortality	0.358

Table 6: Double logistic regression analysis result

Variable	Double logistic regression					
	ICU Indication			Mortality		
	Coeficient	Wald	p	Coeficient	Wald	p
COPD	2.303	6.118	0.013	-	-	-
Albumin	-	-	-	-2.463	4.200	0.040
ESBL	-	-	-	2.793	4.873	0.027

IV. Discussion

Most patients aged >70 years, smokers and having COPD required treatment in ICU and had higher mortality than patients without COPD[13]. Age is one of the most important factors in calculating PORT scores. A high PORT score in patients with COPD is commonly found in older and men[14]. Older age is a predictor of LOS associated with acute infection and abnormal laboratory results (low PaO2 and albumin, sodium imbalance), severity degree of clinical signs (low diastolic blood pressure, respiratory acidosis, high fever, decreased consciousness) or other severity degrees such as pleural effusion, involving multilobar lung abnormalities and a positive blood cultures, or complications such as empyema requiring drainage and treatment in the ICU[15].

The Number of male CAP patients who tends to require ICU treatment are higher and they are also showed a higher mortality rate than female patients. This difference was consistent with animal and human studies indicating that fewer women experienced sepsis or died of pneumonia, but this observation was performed on nosocomial pneumonia. The reasons are still unclear. In animal studies, female hormones are more protective through sepsis[16]. Smoking patients with COPD had higher mortality and required more mechanical ventilation than patients without COPD[13].

The COPD was a risk factor for the occurrence of CAP and ICU cohorts indicating that COPD was often reported as comorbid[17]. The severity degree of COPD and the use of inhaled corticosteroids increased hospitalization risk due to CAP episodes. Patients with severe CAP who were treated with low-dose hydrocortisone for 7 days showed increased output, although the study was terminated earlier due to favorable effects on interim analysis. A

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possible explanation for this finding was an increased adrenal insufficiency up to 60% in patients with severe sepsis or septic shock. Systemic steroid administration in severe CAP patients might improve pituitary-adrenal axis[14].

Hospitalized COPD patients due to CAP were mostly elderly patients. This factor contributed to a high PORT score[14]. In hospitalized CAP patients, hypocapnea and hypercapnea were associated with increased need of ICU care and having high mortality within 30 days[18]. Patient with COPD comorbid treated for CAP showed significantly higher output for ICU care than patients without COPD[17].

Patients with hyperglycemia tended to be dehydrated because of osmotic diuresis and many disruptions to thrombosis and endothelial function, such as slow chemotaxis, phagocytosis disorders, and decreased micro biocidal capacity. The CAP patients with DM comorbid would recover lately by the factors mentioned above thus it would extend LOS. Hospitalized patients with glucose >11 mmol/l had a slower oxygen saturation in order to be normal compared to glucose ≤11 mmol/l (83% vs 90%), therefore patients experienced longer hypoxemia[19]. Mild acute hyperglycemia patients had significantly increased death risk within 90 days and this risk increased if serum glucose ≥4 mmol/l[20]. Hyperglycemia interfered the function of hypoxia-inducible factor 1-alpha which would cause proteosomal degradation resulting in cellular response due to peptide bonding on discontinuous protein, and the end result was cell and tissue hypoxia[21].

In this study we found 2 patients died due to cardiac event. Inflammation played an important role in the pathogenesis of coronary artery disease. Increased concentrations of pro-inflammatory cytokines produced by systemic infection were triggered by endothelial dysfunction, unstable atheroma, and plaque rupture. It could be estimated that the risk of acute myocardial infarction (AMI) was higher in patients with infections associated with strong inflammatory responses (such as respiratory infections) than patients with mild inflammatory responses (such as urinary tract infections). In hospitalized CAP patients, the high levels of pro-inflammatory cytokines were associated with severe disease. If cytokine levels and inflammatory responses had relationship with airway infections and AMI, then the incidence of AMI should be increased in patients with severe CAP. This allowed CAP patients with KV comorbid to have longer LOS and higher mortality due to severe sepsis requiring treatment in ICU[22].

In hospitalized CAP patients, anemia was commonly found and associated with increased LOS and mortality. There was an increase in the manipulation of Hb in hospitalized patients with interventions such as thrombosis transfusions, recombinant human erythropoietin, and blood substitution. Anemia increased in severe disease and more common in comorbid and women with poor outcomes. Moderate to severe anemia (Hb ≤ 10 g / dl) was associated with prolonged LOS and increased mortality within 90 days[23].

Hospitalized CAP patients with hypoalbuminemia had high morbidity and mortality. Low albumin serum at hospital admission time increased complications risk, including empyema, cardiac events, kidney failure, and nosocomial infections. In addition, low albumin levels were also associated with prolonged LOS, increased care in ICU, requiring mechanical ventilation, and increased mortality within 30 days[24]. Albumin played an important role in maintaining physiological homeostasis, including maintaining normal colloidal osmotic pressure, transporting endogenous materials, and scavenging oxidants[25]. Low albumin correlated with nutritional status of patients and it was a significant risk factor in mortality where albumin <2.2 mg/dl was significantly associated with mortality[26].

Antibiotics administration delay was associated with an increased risk of death, and the delay was commonly found in ESBL groups. Another study showed the elongation of LOS in ESBL-infected cohorts and these findings

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were counterintuitive. A possible explanation was the high mortality in the ESBL could not be a representative comparison of LOS[27]. Risk factors for colonization of E. coli and Klebsiella spp. that produced ESBL at the admission of ICU were age >60 years, comorbid, use of piperacillin-tazobactam and vancomycin in the previous hospital. Carbapenem was an empirical therapy for patients with ESBL risk[28].

Basically, empiric antimicrobial therapy should be appropriate in patients with severe infections, especially those with septic shock. Treatment factors might contribute to adverse outcomes of resistant pathogens patients. These factors included decreased effectiveness, increased drug toxicity, improper doses of antimicrobial agent available for treatment, delayed treatment or absence of microbiologically effective antimicrobials, increased need for surgery and other procedures resulting from the infection[29]. Administration of antibiotics <8 hours from hospital admission was associated with decreased mortality and LOS among random samples of older patients who did not receive antibiotics prior to admission[30].

A study found that PORT scores predicted hospital mortality in 30 days was relatively good for CAP patients[31]. The observational study found that PORT score was an independent factor related to treatment in ICU (OR 5.35, 95% CI 1.90-15.06, p = 0.002)[25].

V. Conclusion

There was a significant relationship between COPD comorbid, DM, and PORT score through indication of ICU care. The COPD comorbid was the most dominant independent factor through indication of care in ICU. Albumin and ESBL germs were the same dominant independent factor for mortality.

References

[1] Lutfiyya MN, Henley E, Chang LF, Reyburn SW. Diagnosis and treatment of community-acquired pneumonia. American family physician. 2006;73(3):442-50.

[2] Prasad R. Community acquired pneumonia: clinical manifestations. The Journal of the Association of Physicians of India. 2012;60 Suppl:10-2.

[3] Goetz MB, Rhew, D.C., Torres, A. Pyogenic bacterial pneumonia, lung abscess, and empyema. 4th ed. Nadel's Ma, editor2005.

[4] Paganin F, Lilienthal F, Bourdin A, Lugagne N, Tixier F, Génin R, Yvin JL.. Severe community-acquired pneumonia: assessment of microbial aetiology as mortality factor. The European respiratory journal. 2004;24(5):779-85. https://doi.org/10.1183/09031936.04.00119503

[5] Christ-Crain M, Stolz D, Bingisser R, Müller C, Miedinger D, Huber PR, Zimmerli W, Harbarth S, Tamm M, Müller B. Procalcitonin guidance of antibiotic therapy in community-acquired pneumonia: a randomized trial. American journal of respiratory and critical care medicine. 2006;174(1):84-93. https://doi.org/10.1164/rccm.200512-1922OC

[6] Soedarsono. Pneumonia In Wibisono MJ, Winariani, Hariadi S (eds), Buku Ajar Ilmu Penyakit Paru, Departemen Ilmu Penyakit Paru FK UNAIR-RSUD Dr.Soetomo Surabaya. 2010.

[7] Vandijck DM, Decruyenaere JM, Depuydt PO, Blot SI. Community-acquired versus nosocomial Klebsiella pneumonia bacteremia: clinical features, treatment outcomes, and clinical implication of antimicrobial resistance. Journal of Korean medical science. 2007;22(4):770-1.

[8] Huang HH, Zhang YY, Xiu QY, Zhou X, Huang SG, Lu Q, Wang DM, Wang F. Community-acquired pneumonia in Shanghai, China: microbial etiology and implications for empirical therapy in a prospective study of 389 patients. European journal of clinical microbiology & infectious diseases:

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official publication of the European Society of Clinical Microbiology. 2006;25(6):369-74. https://doi.org/10.1007/s10096-006-0146-7

[9] Bansal S, Kashyap S, Pal LS, Goel A. Clinical and bacteriological profile of community acquired pneumonia in Shimla, Himachal Pradesh. The Indian journal of chest diseases & allied sciences. 2004;46(1):17-22.

[10] Hawkey PM. Prevalence and clonality of extended-spectrum beta-lactamases in Asia. Clinical microbiology and infection : the official publication of the European Society of Clinical Microbiology and Infectious Diseases. 2008;14 Suppl 1:159-65. https://doi.org/10.1111/j.1469-0691.2007.01855.x

[11] Turner PJ. Extended-spectrum beta-lactamases. Clinical infectious diseases : an official publication of the Infectious Diseases Society of America. 2005;41 Suppl 4:S273-5. https://doi.org/10.1086/430789

[12] Bartlett JG, Mundy, L.M. Current concepts: community-acquired pneumonia. The New England journal of medicine. 1995;333:1618–1624. https://doi.org/10.1056/NEJM199512143332408

[13] Rello J, Rodriguez A, Torres A, Roig J, Sole-Violan J, Garnacho-Montero J, de la Torre MV, Sirvent JM, Bodi M. Implications of COPD in patients admitted to the intensive care unit by community-acquired pneumonia. The European respiratory journal. 2006;27(6):1210-6. https://doi.org/10.1183/09031936.06.00139305

[14] Snijders D, van der Eerden M, de Graaff C, Boersma W. The influence of COPD on mortality and severity scoring in community-acquired pneumonia. Respiration; international review of thoracic diseases. 2010;79(1):46-53. https://doi.org/10.1159/000213757

[15] Suter-Widmer I, Christ-Crain M, Zimmerli W, Albrich W, Mueller B, Schuetz P; ProHOSP Study Group. Predictors for length of hospital stay in patients with community-acquired pneumonia: results from a Swiss multicenter study. BMC pulmonary medicine. 22012; 12:21 https://doi.org/10.1186/1471-2466-12-21

[16] Kaplan V, Angus DC, Griffin MF, Clermont G, Scott Watson R, Linde-Zwirble WT. Hospitalized community-acquired pneumonia in the elderly: age- and sex-related patterns of care and outcome in the United States. American journal of respiratory and critical care medicine. 2002;165(6):766-72. https://doi.org/10.1164/ajrccm.165.6.2103038

[17] Restrepo MI, Mortensen EM, Pugh JA, Anzueto A. COPD is associated with increased mortality in patients with community-acquired pneumonia. The European respiratory journal. 2006;28(2):346-51. https://doi.org/10.1183/09031936.06.00131905

[18] Laserna E, Sibila O, Aguilar PR, Mortensen EM, Anzueto A, Blanquer JM, Sanz F, Rello J, Marcos PJ, Velez MI, Aziz N, Restrepo MI. Hypocapnia and hypercapnia are predictors for ICU admission and mortality in hospitalized patients with community-acquired pneumonia. Chest. 2012;142(5):1193-9. https://doi.org/10.1378/chest.12-0576

[19] McAlister FA, Majumdar SR, Blitz S, Rowe BH, Romney J, Marrie TJ. The relation between hyperglycemia and outcomes in 2,471 patients admitted to the hospital with community-acquired pneumonia. Diabetes care. 2005;28(4):810-5. https://doi.org/10.2337/diacare.28.4.810

[20] Lepper PM, Ott S, Nuesch E, von Eynatten M, Schumann C, Pletz MW, et al. Serum glucose levels for predicting death in patients admitted to hospital for community acquired pneumonia: prospective cohort study. Bmj. 2012;344:e3397. https://doi.org/10.1136/bmj.e3397

[21] Catrina SB, Okamoto K, Pereira T, Brismar K, Poellinger L. Hyperglycemia regulates hypoxia-inducible factor-1alpha protein stability and function. Diabetes. 2004;53(12):3226-32. https://doi.org/10.2337/diabetes.53.12.3226

[22] Ramirez J, Aliberti S, Mirsaeidi M, Peyrani P, Filardo G, Amir A, Moffett B, Gordon J, Blasi F, Bordon J. Acute myocardial infarction in hospitalized patients with community-acquired pneumonia. Clinical infectious diseases: an official publication of the Infectious Diseases Society of America. 2008;47(2):182-7. https://doi.org/10.1086/589246

DOI: 10.37200/IJPR/V24I2/PR200734
Received: 05 Jan 2020 | Revised: 20 Jan 2020 | Accepted: 30 Jan 2020

[23] Reade MC, Weissfeld L, Angus DC, Kellum JA, Milbrandt EB. The prevalence of anemia and its association with 90-day mortality in hospitalized community-acquired pneumonia. BMC pulmonary medicine. 2010;10:15. https://doi.org/10.1186/1471-2466-10-15

[24] Viasus D, Garcia-Vidal C, Simonetti A, Manresa F, Dorca J, Gudiol F, Carratalà J. Prognostic value of serum albumin levels in hospitalized adults with community-acquired pneumonia. The Journal of infection. 2013;66(5):415-23. https://doi.org/10.1016/j.jinf.2012.12.007

[25] Ugajin M, Yamaki K, Iwamura N, Yagi T, Asano T. Blood urea nitrogen to serum albumin ratio independently predicts mortality and severity of community-acquired pneumonia. International journal of general medicine. 2012;5:583-9. https://doi.org/10.2147/IJGM.S33628

[26] Irfan M, Hussain SF, Mapara K, Memon S, Mogri M, Bana M, Malik A, Khan S, Khan NA. Community acquired pneumonia: risk factors associated with mortality in a tertiary care hospitalized patients. JPMA The Journal of the Pakistan Medical Association. 2009;59(7):448-52.

[27] Melzer M, Petersen I. Mortality following bacteraemic infection caused by extended spectrum beta-lactamase (ESBL) producing E. coli compared to non-ESBL producing E. coli. The Journal of infection. 2007;55(3):254-9. https://doi.org/10.1016/j.jinf.2007.04.007

[28] Harris AD, McGregor JC, Johnson JA, Strauss SM, Moore AC, Standiford HC, Hebden JN, Morris JG Jr. Risk factors for colonization with extended-spectrum beta-lactamase-producing bacteria and intensive care unit admission. Emerging infectious diseases. 2007;13(8):1144-9. https://doi.org/10.3201/eid1308.070071

[29] Schwaber MJ, Carmeli Y. The effect of antimicrobial resistance on patient outcomes: importance of proper evaluation of appropriate therapy. Critical care. 2009;13(1):106. https://doi.org/10.1186/cc7136

[30] Houck PM, Bratzler DW, Nsa W, Ma A, Bartlett JG. Timing of antibiotic administration and outcomes for Medicare patients hospitalized with community-acquired pneumonia. Archives of internal medicine. 2004;164(6):637-44. https://doi.org/10.1001/archinte.164.6.637

[31] Abisheganaden J, Ding YY, Chong WF, Heng BH, Lim TK. Predicting mortality among older adults hospitalized for community-acquired pneumonia: an enhanced confusion, urea, respiratory rate and blood pressure score compared with pneumonia severity index. Respirology. 2012;17(6):969-75. https://doi.org/10.1111/j.1440-1843.2012.02183.x

[32] Hwazenamerabdalnabi, J., Jasimm, A., Altameme Molecular screening of E.Colibiofilm and anantibiofilm activity ofcapparisspinosa L extracts.(2018) International Journal of Pharmaceutical Research, 10 (4), pp. 528-532. https://www.scopus.com/inward/record.uri?eid=2-s2.0-85062385455&doi=10.31838%2fijpr%2f2018.10.04.105&partnerID=40&md5=6b066b3c50a5b76c142f205fd7e85b08

[33] K, m. S. K., alias, . M. & r., . S. K. (2018) a review on novel uses of vitamin e. Journal of Critical Reviews, 5 (2), 10-14. doi:10.22159/jcr.2018v5i2.24282

[34] Ghosh A, Ghosh T. "Herbal Drugs of Abuse." Systematic Reviews in Pharmacy 1.2 (2010), 141-145. Print. doi:10.4103/0975-8453.75060

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