Risk factors predicting outcome in patients with pneumonia in Al-Ain, United Arab Emirates

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ABSTRACT

Objective: To determine the predictive value of commonly used clinical and laboratory factors for mortality in patients with pneumonia in the Arab world.

Methods: We retrospectively analyze the data collected from all inpatients over the age of 16 years with a diagnosis of pneumonia in Tawam Hospital, Al-Ain, United Arab Emirates between the years 1997 and 2002. Patients were grouped into those who survived and those who died in the hospital. Clinical and laboratory factors on admission were used to predict outcome using simple, and multiple logistic regression analyses.

Results: Among the 236 patients admitted, 122 were females (age 56.9 ± 23 years), and 114 males (age 58.5 ± 23 years). The 30-day mortality rate was 10%. The most common comorbid risk factors were diabetes mellitus in 23.7% and chronic obstructive pulmonary disease in 19.5%. Of the 236 patients, 145 had sputum culture on admission. Simple logistic regression analysis showed increasing age, presence of comorbidity, low systolic blood pressure, confused mental status, low serum albumin, high serum creatinine, raised blood urea nitrogen and raised partial pressure of carbon dioxide at the time of admission were associated with higher mortality. On the Stepwise-multilogistic regression analysis, the most significant factors influencing mortality were: older age, altered mental status, low systolic blood pressure, low serum albumin and raised serum creatinine. Using a scoring system developed in the presence or absence of these risk factors, a score of ≥100 predicted high risk for mortality.

Conclusion: The in-hospital mortality rate for pneumonia was 10%. Older age, altered mental status, low systolic blood pressure, low serum albumin concentration and raised serum creatinine at admission were predictive of poor outcome in this cohort of patients.

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Pneumonia is a common problem worldwide and the reported mortality rate for hospitalized patients with pneumonia varies from 10-25%.[1] Several investigators have sought clinical and biochemical indices on admission in order to predict the outcome. Based on these predictive factors, patients have been stratified as low, moderate and high risk for survival.[2-4] However, the utility of pneumonia management guidelines based on these criteria has been questioned.[5] Furthermore, it has been suggested that since circumstances may vary between countries, admission indices should be investigated in individual countries in order to develop appropriate, targeted management guidelines.[6] In this context, there is a paucity of literature from the Arab world.[7] Therefore, we retrieved data on all admitted patients

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to a university hospital over a 5-year period in order to determine the predictive value of commonly used clinical and laboratory factors for mortality.

Methods. In this retrospective chart review, data were collected from all in-patients over the age of 16 years, admitted to Tawam Hospital, Al-Ain, United Arab Emirates (UAE) with a diagnosis of pneumonia between the years 1997 and 2002. The cases were identified from the medical records using the International Classification of Diseases code ICD-9-CM for community-acquired pneumonia. Two independent physicians scrutinized the charts to confirm the diagnosis of pneumonia. A standard form was used to collect patient demographics, clinical history, vital signs, clinical examination findings at the time of admission and the results of the laboratory investigations reported within 24 hours of admission. Of the 236 patients, 28 had pneumonia identified with one or more episode on admission. From these 28 patients, only data from the last admission were included in order to avoid inaccuracy in statistical analysis.

The following clinical factors at the time of admission were documented: age, gender, presence of comorbidity, altered mental status, respiratory rate, systolic and diastolic blood pressure (BP), temperature and pulse rate. The laboratory indices recorded on admission were: total white blood count (WBC), blood urea nitrogen (BUN), serum sodium, glucose, arterial pH, partial pressure of oxygen (PO_2), partial pressure of carbon dioxide (PCO_2) and chest x-ray evidence of multiple lobe involvement and presence of pleural effusion. The criteria for mortality were defined as any death occurring within 30 days of hospitalization as a result of pneumonia or to any complication related to the pneumonia. Approval was obtained from the Tawam Hospital Ethics Committee and the Faculty of Medicine and Health Sciences Research Review Committee.

Statistical analysis. In order to determine the significant risk factors for mortality, simple logistic regression analyses were run between outcome and each of the following variables: age, gender, systolic BP, diastolic BP, pulse, respiratory rate, temperature, altered mental status, number of comorbidities, serum albumin, BUN, creatinine, sodium, pH, glucose, PO_2, PCO_2, total WBC count, and chest x-ray findings.

A backward stepwise logistic regression analysis was then run to determine the subset of significant factors that "best" predict mortality. The response variable was "outcome" (dead versus alive) and the predictors were the significant factors derived from the simple logistic regression analysis. The variable "PCO_2" was not considered in this step, as it was measured in only 27% of the sample subjects. The Hosmer-Lemeshow goodness-of-fit test had a *p*-value = 0.357, thus, suggesting that the fitted logistic model fitted the data well.

The "best" subset of predictors of mortality was used to derive a simple rule for predicting subjects were at higher risk of mortality. The rule was derived as follows: the continuous variables from the multilogistic regression (age, systolic BP, serum albumin and creatinine) were dichotomized into age greater than or equal to 65 years, systolic BP less than 90 mm Hg, serum albumin less than or equal to 30 g/L and serum creatinine greater than or equal 133 mmol/L. A multiple logistic regression of outcome versus these 5 dichotomous variables and altered mental status was run. The predictive scores for the variables: systolic BP, altered mental status, serum albumin and creatinine were obtained by dividing the logistic regression coefficient of each of these variables by the coefficient of age, multiplying by 10 then rounding to the nearest multiple of 5.

From these predictive scores, sensitivity and specificity were calculated. However, it is well known that probabilities of correct classifications (example specificity and sensitivity) computed from the sample data used to derive the prediction rule tend to overestimate the true probabilities of correct classifications. To correct these estimation biases, we used a bootstrapping technique based on 200 bootstrap samples to approximate the estimation biases.[8]

Results. Among the 236 patients, 122 were females and 114 males. The mean age (± SD) of the population was 57.7 years ± 22.8. The age range varied from 16 years to 99 years. The ethnicity was: UAE nationals 75.8%, other Arab nationals 22.5% and patients of Asian origin 1.7%. The 30-day mortality rate was 10%. The most common comorbid risk factors were diabetes in 23.7% and chronic obstructive pulmonary disease in 19.5%, cerebro vascular accidents in 9%, renal failure in 7%, heart failure in 7%, HIV in 1%. Thirty-five percent of the population did not have any comorbid risk factors.

The significant predictors of mortality from simple logistic regression analysis (**Table 1**) were: increasing age, low systolic BP, high respiratory rate, impaired mental status, low serum albumin, high serum creatinine, raised BUN and raised PCO_2 at the time of admission to hospital. The most significant factors affecting mortality in multilogistic regression analysis were: older age, altered mental status, low systolic BP, low serum albumin and raised serum creatinine (**Table 2**). **Table 3** shows the coefficients of the 5

Table 1 - Simple logistic regression of outcome versus putative risk factors.

Factor	N	Coefficient	*P*-value*	Odds ratio	95% CI for odds ratio
Age	236	0.04	<0.001	1.05	1.02 – 1.07
Gender†	236	0.56	0.203	1.76	0.73 – 4.24
Systolic blood pressure	236	-0.03	0.002	0.97	0.95 – 0.99
Diastolic blood pressure	236	-0.01	0.407	0.99	0.96 – 1.02
Pulse	236	0.01	0.546	1.01	0.99 – 1.03
Respiratory rate	236	0.05	0.023	1.05	1.01 – 1.10
Temperature	236	-0.31	0.084	0.73	0.50 – 1.08
Altered mental status‡	236	1.72	0.009	5.57	1.72 – 18
Albumin	215	-0.16	<0.001	0.85	0.78 – 0.93
Blood urea nitrogen	215	0.07	0.001	1.07	1.03 – 1.11
Creatinine	215	0.02	<0.001	1.02	1.01 – 1.02
Sodium	215	0.03	0.165	1.04	0.98 – 1.10
Number of comorbidity	236	0.48	0.061	1.62	0.99 – 2.65
Arterial pH	64	-0.07	0.507	0.93	0.64 – 1.36
Serum glucose	215	-0.01	0.379	0.99	0.96 – 1.02
Arterial PO_2	64	0.00	0.766	1	0.99 – 1.02
Arterial PCO_2	64	0.07	0.009	1.07	1.01 – 1.13
Total WBC count	236	0.01	0.694	1.01	0.95 – 1.08
Chest x-ray**	236		0.34		
Infiltrate		0.78		2.19	0.48 – 10.04
Effusion		1.23		3.42	0.27 – 43.70
Infiltrate and effusion		1.57		4.82	0.81 – 28.86

*Based on likelihood ratio test (Omnibus test in SPSS output), †Reference category - Female, ‡Reference category - normal, **Reference category - Nil

PO_2 - partial pressure of oxygen, PCO_2 - partial pressure of carbon dioxide, WBC - white blood count, CI - confidence interval

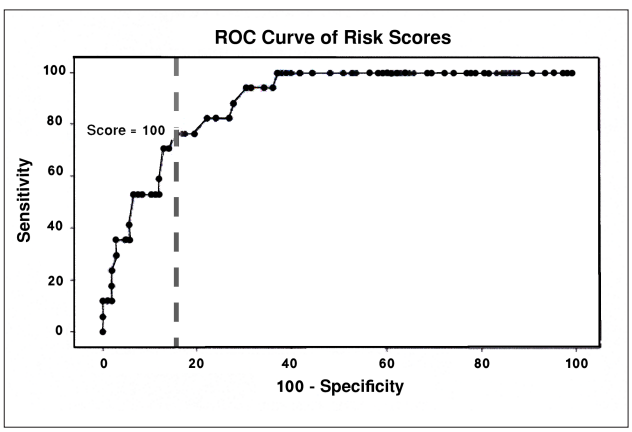

Figure 1 - Provides the Receiver Operator Characteristics of predictive scores. The response variable was "Outcome" (dead versus alive) and the predictors were age, systolic blood pressure, altered mental status, serum albumin and serum creatinine. The optimum cutoff levels was selected to provide the maximum sensitivity and specificity.

Table 2 - Results of stepwise logistic regression - "best" subset of predictors of outcome.

Predictor	Coefficient	*P*-value
Age	0.073	0.029
Systolic blood pressure	-0.081	0.003
Altered mental status*	5.002	0.002
Albumin	-0.133	0.023
Creatinine	0.021	0.006

*Reference category - normal

Table 3 - Coefficients of significant predictors in logistic regression.

Predictors	Coefficients	Predictive scores
Age ≥65 yrs	0.94	-
Systolic blood pressure <90 mm Hg	2.988	30
Altered mental status (Confused)	3.457	35
Albumin ≤30 g/L	1.292	15
Creatinine >133 mmol/L	2.383	25

predictive factors from multiple logistic regression. The optimal cutoff limit for age at 65 years as a predictor for mortality was derived from the Receiver Operator Characteristics (ROC) analysis. **Figure 1** shows the ROC curve developed for predictive factors of mortality. The optimal cutoff level for classifying patients into low risk and high risk was 100. A score of 100 corresponds to an observed cumulative mortality of approximately 5%. Validation of this predictive scoring system using bootstrapping technique yielded a specificity 79% and sensitivity 66%.

Discussion. In this first retrospective analysis of data from patients admitted with pneumonia in an Arab country, we have identified 7 independent predictors of mortality besides age using simple logistic regression. These factors were: low systolic BP, high respiratory rate, altered mental status, low serum albumin, raised BUN and raised serum creatinine levels. However, stepwise-multilogistic regression revealed that only 5 of these factors were important in predicting mortality in this cohort of patients with pneumonia. These factors were: age more than 65 years, low systolic BP, presence of altered mental status, low serum albumin level and raised serum creatinine concentration on admission. We have also successfully used the bootstrap method described by Efron and Tibshirani[8] for validating the outcomes from this cohort of patients.

The presence of comorbidity has been established as a significant predictor of mortality in patients with pneumonia studies carried out in other countries. Although our results in this regard were not significant at the 5% level, there was a trend for comorbidity to be predictor for mortality in this cohort of patients.[9-11] The most common comorbid illness in our series was diabetes mellitus, which reflects the high prevalence of this disorder in the UAE. Interestingly, alcoholism, chronic liver disease and acquired immune deficiency syndrome were rare in this cohort compared to other published reports.[3,12] Furthermore in the present study, low systolic BP in patients with pneumonia on admission to hospital has been shown to predict a poor outcome in previous reports.[2,10,13] While a low diastolic BP has been reported to be a major predictor of death in pneumonia in some studies,[14-17] this association was not seen in the present study.

Altered mental status has been consistently shown to be a reliable predictor of poor outcome in pneumonia[2,3,15-17] and our results agree with this observation. Altered mental status in pneumonia is presumed to represent the clinical effects systemic inflammatory response in patients with pneumonia.

Although liver disease has been recognized as a comorbid condition affecting the outcome in pneumonia in some reports,[18,19] low serum albumin has been recently identified as an independent predictor of mortality.[20] To insure that these observed effects of low serum albumin on odds of survival are truly due to pneumonia rather than a confounding factor like comorbid conditions, we ran a multiple logistic regression of outcome versus serum albumin concentration for patients with different types of comorbid illness. As there was no significant association between serum albumin concentrations in patients with different coexisting illness, low serum albumin appears to be an independent predictor of mortality in this cohort.

Sepsis and infection such as pneumonia are associated with increased production of early phase reactive proteins such as C-reactive protein, Mannan-binding lectin and lipopolysaccharide-binding protein by the liver.[21-24] All of these are essential in the innate immunity.[25] Furthermore, low serum concentrations of lipopolysaccharide-binding protein are associated with a high mortality rate in human sepsis.[24] In this setting, it is possible that patients with pneumonia and low serum albumin represent a cohort with poor liver function and by virtue of this, are unable to mount an appropriate innate immune response to infections and therefore, are at higher risk of dying from pneumonia.

Interestingly, the incidence of parapneumonic pleural effusion was very low in this cohort compared to other published series.[26] Furthermore, it is of interest that the incidence of empyema was low compared to other reports.[26,27]

The 30-day mortality from pneumonia in this dominantly Arab population was 10%. Older age, altered mental status, low systolic BP, low serum albumin concentration and raised serum creatinine level at admission were predictive of poor outcome in this cohort of patients. Compared to other published series, the factors predicting mortality in pneumonia appear to be somewhat different. The frequencies of parapneumonic effusion and empyema were very low. Although the results of this study have been validated using repeated sampling procedure described in bootstrap methodology, a prospective validation study of the established risk factors for mortality in patients admitted with pneumonia is warranted in this population.

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References

1. Bartlett JG, Mundy LM. Community-acquired pneumonia. ***N Engl J Med*** 1995; 333: 1618-1624.

2. de Castro FR, Torres A. Optimizing treatment outcomes in severe community-acquired pneumonia. ***Am J Respir Med*** 2003; 2: 39-54.
3. Fine MJ, Auble TE, Yealy DM, Hanusa BH, Weissfeld LA, Singer DE, et al. A prediction rule to identify low-risk patients with community-acquired pneumonia. ***N Engl J Med*** 1997; 336: 243-250.
4. Leroy O, Devos P, Guery B, Georges H, Vandenbussche C, Coffinier C, et al. Simplified prediction rule for prognosis of patients with severe community-acquired pneumonia in ICUs. ***Chest*** 1999; 116: 157-165.
5. Woodhead M. Community-acquired pneumonia in Europe: causative pathogens and resistance patterns. ***Eur Respir J Suppl*** 2002; 36: 20s-27s.
6. Woodhead M. Community-acquired pneumonia guidelines: much guidance, but not much evidence. ***Eur Respir J*** 2002; 20:1-3.
7. Kurashi NY, Al Hamdan A, Ibrahim EM, Al Idrissi HY, Al Bayari TH. Community acquired acute bacterial and atypical pneumonia in Saudi Arabia. ***Thorax*** 1992; 47: 115-118.
8. Efron B, Tibshirani RJ. An introduction to the bootstrap. New York: Chapman and Hall; 1993.
9. Almirall J, Bolibar I, Balanzo X, Gonzalez CA. Risk factors for community-acquired pneumonia in adults: a population-based case-control study. ***Eur Respir J*** 1999; 13: 349-355.
10. Fine MJ, Hough LJ, Medsger AR, Li YH, Ricci EM, Singer DE, et al. The hospital admission decision for patients with community-acquired pneumonia. Results from the pneumonia Patient Outcomes Research Team cohort study. ***Arch Intern Med*** 1997; 157: 36-44.
11. Moine P, Vercken JB, Chevret S, Chastang C, Gajdos P. Severe community-acquired pneumonia. Etiology, epidemiology, and prognosis factors. French Study Group for Community-Acquired Pneumonia in the Intensive Care Unit. ***Chest*** 1994; 105: 1487-1495.
12. Ruiz M, Ewig S, Torres A, Arancibia F, Marco F, Mensa J, et al. Severe community-acquired pneumonia. Risk factors and follow-up epidemiology. ***Am J Respir Crit Care Med*** 1999; 160: 923-929.
13. Angus DC, Marrie TJ, Obrosky DS, Clermont G, Dremsizov TT, Coley C, et al. Severe community-acquired pneumonia: use of intensive care services and evaluation of American and British Thoracic Society Diagnostic criteria. ***Am J Respir Crit Care Med*** 2002; 166: 717-723.
14. Lim WS, Lewis S, Macfarlane JT. Severity prediction rules in community acquired pneumonia: a validation study. ***Thorax*** 2000; 55: 219-223.
15. Neill AM, Martin IR, Weir R, Anderson R, Chereshsky A, Epton MJ, et al. Community acquired pneumonia: aetiology and usefulness of severity criteria on admission. ***Thorax*** 1996; 51: 1010-1016.
16. Kamath A, Pasteur MC, Slade MG, Harrison BD. Recognising severe pneumonia with simple clinical and biochemical measurements. ***Clin Med*** 2003; 3: 54-56.
17. Farr BM, Sloman AJ, Fisch MJ. Predicting death in patients hospitalized for community-acquired pneumonia. ***Ann Intern Med*** 1991; 115: 428-436.
18. Ewig S, Schafer H, Torres A. Severity assessment in community-acquired pneumonia. ***Eur Respir J*** 2000; 16: 1193-1201.
19. Espana PP, Capelastegui A, Quintana JM, Soto A, Gorordo I, Garcia-Urbaneja M, et al. A prediction rule to identify allocation of inpatient care in community-acquired pneumonia. ***Eur Respir J*** 2003; 21: 695-701.
20. Lim WS, van der Eerden MM, Laing R, Boersma WG, Karalus N, Town GI, et al. Defining community acquired pneumonia severity on presentation to hospital: an international derivation and validation study. ***Thorax*** 2003; 58: 377-382.
21. Smith RP, Lipworth BJ. C-reactive protein in simple community-acquired pneumonia. ***Chest*** 1995; 107: 1028-1031.
22. Masia M, Gutierrez F, Llorca B, Navarro JC, Mirete C, Padilla S, et al. Serum concentrations of lipopolysaccharide-binding protein as a biochemical marker to differentiate microbial etiology in patients with community-acquired pneumonia. ***Clin Chem*** 2004; 50: 1661-1664.
23. Mirete C, Gutierrez F, Masia M, Ramos JM, Hernandez I, Soldan B. [Usefulness of acute-phase proteins in community-acquired pneumonia]. ***Med Clin (Barc)*** 2004; 122: 245-247.
24. Zweigner J, Gramm HJ, Singer OC, Wegscheider K, Schumann RR. High concentrations of lipopolysaccharide-binding protein in serum of patients with severe sepsis or septic shock inhibit the lipopolysaccharide response in human monocytes. ***Blood*** 2001; 98: 3800-3808.
25. Medzhitov R, Janeway C, Jr. Innate immunity. ***N Engl J Med*** 2000; 343: 338-344.
26. Light RW, Girard WM, Jenkinson SG, George RB. Parapneumonic effusions. ***Am J Med*** 1980; 69: 507-512.
27. Joseph J, Badrinath P, Basran GS, Sahn SA. Is the pleural fluid transudate or exudate? A revisit of the diagnostic criteria. ***Thorax*** 2001; 56: 867-870.