Print ISSN: 2321-6379
Online ISSN: 2321-595X
DOI: 10.17354/ijss/2017/345

Original Article

Study of Lab Parameters Predicting Post-discharge Mortality after Admission for Community-acquired Pneumonia: A Prospective Tertiary Hospital Care Based Study

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Abstract

Introduction: There are considerable morbidity and mortality following discharge of patients admitted as community-acquired pneumonia (CAP). There is very scarce data about follow-up of these patients after they are discharged from the hospital.

Aims and Objectives: To study the lab parameters predicting post-discharge mortality following admission for CAP on follow-up.

Materials and Methods: A prospective cohort of patients presenting as CAP admitted in our institute (Sher-i-Kashmir Institute of Medical Sciences) was recruited from October 2008 to April 2010.

Results: Our study comprised 153 patients of CAP with median follow-up of 397 days. Mean age of patients was 61.31 ± 16.49 years. 99 (62.8%) were male and 54 patients were females. From total of 153 patients 34 (22.22%) patients died at median follow-up of 397 days. Hypoalbuminemia (P = 0.03), increased blood urea nitrogen (BUN) (P = 0.00), serum creatinine >1.5 mg/dl, hyperglycemia (>250 mg/dl) (P = 0.02), pH <7.35 (P = 0.01), bilateral involvement on chest X-ray (P = 0.01), and higher pneumonia severity index (PSI) class (P = 0.0001) were found to be significantly associated with mortality on follow-up. We could not ascertain any relation between particular microbial etiology and mortality on follow-up.

Conclusion: There is considerable mortality following discharge of patients admitted with CAP. Hypoalbuminemia, increased BUN, creatinine, blood sugar, low pH and higher PSI class can be used as factors in predicting which patients will have a poor outcome after discharge from the hospital.

Key words: Lab parameters, Pneumonia, Mortality

INTRODUCTION

Considering the importance of community-acquired pneumonia (CAP) it is remarkable how little is known about what happen to patients after they are discharged from the hospital. Patients who survive an episode of CAP in intensive care units (ICUs) have greater mortality after discharge from hospital than age-matched control subjects.[1-16] Observations by few investigators indicate that only independent predictors of mortality after discharge were mental obtundation, comorbid illnesses and decreased hematocrit. Thus, a possibility that CAP may present a sentinel event for many life-limiting diseases and hence should alert a treating physician for a close and careful follow-up. It appears that increased risk of death persists for several years after an episode of pneumonia; specific features of pneumonia episode may alert clinicians to focus particular attention on the longer term prognosis of certain patients. Although the cause of the decreased long-term survival is not yet clear, it may be that the systemic inflammatory response produced by CAP accelerates the natural course of medical

Access this article online

www.ijss-sn.com

Month of Submission : 05-2017
Month of Peer Review : 06-2017
Month of Acceptance : 07-2017
Month of Publishing : 07-2017

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comorbidities such as atherosclerosis. This hypothesis is bolstered by a recent study that showed reduced long-term survival in CAP+ patients who were clinically cured but had increased interleukin 6 and interleukin 10 levels at the time of hospital discharge. In apparently healthy older individuals, low-grade inflammation occurs is associated with increased risk of CAP.[17] Once pneumonia, inflammatory marker concentrations are several times higher.[18] Very little is known about factors predicting long-term mortality following an episode of CAP. Our study was designed to analyze what lab parameters lead to decrease in long-term survival, so as to identify patients at high risk of mortality on follow-up and to formulate better follow-up of these patients which in turn will reduce long-term mortality.

Aims and Objectives

To study the lab predictors of mortality after hospitalization in patients with CAP.

MATERIALS AND METHODS

Study Design

A prospective cohort of patients admitted in our institute (Sher-i-Kashmir Institute of Medical Sciences) was recruited from October 2008 to April 2010. The subjects were enrolled only after written informed consent. Patients were followed for mortality and morbidity closely by noting their home addresses, cell/telephone numbers.

Inclusion Criteria

All patients presenting with CAP were included in the study. CAP was defined as an acute illness (fewer than 14 days of symptoms), the presence of new chest infiltrates as confirmed by a radiologist or pulmonary critical care physician, and clinical features suggestive of acute pneumonia. The clinical features required were one of Group A (fever >37.8°C, hypothermia <36°C, cough and sputum production) or two of B (dyspnea, pleuritic pain physical findings suggestive of lung consolidation, and leukocyte count >12,000 or <4000). These criteria are consistent with the published guidelines of CAP.[19]

Exclusion Criteria

1. Patients with severe immunodeficiency as defined by the Centers for Disease Control Criteria for patients with acquired immune deficiency syndrome;[20]
2. Patients receiving chemotherapy in the past 60 days;
3. Patients receiving treatment with corticosteroids equivalent to prednisolone at more than 20 mg/day for more than 14 days;
4. Patients receiving immunosuppression after organ transplantation;
5. Patients receiving cyclosporine, cyclophosphamide, or azathioprine;
6. Non-ambulatory patients and;
7. Patients hospitalized within the past 30 days.

All patients who died within 30 days of hospital discharge were excluded from the study. Mortalities after 30 days of hospital discharge were taken into account.

Data Collection

The variables of interest which were results of tests as ordered by a treating physician such as blood glucose levels, blood urea, serum creatinine, complete blood count, liver function tests, electrocardiogram, X-ray chest, ultrasound abdomen, and cultures as ordered by the treating physician were recorded pneumonia severity index (PSI) score was calculated as described by Fine *et al.*[4]

Statistical Calculations

Statistical calculations were performed with SPSS 17 statistical package. Univariate analysis using Chi-square tests or Fisher exact tests were used when the variable of interest was categorical. Cox regression modeling was used for multivariate analysis with models using all significant interactions. All *P* values were taken as two-tailed with a value below 0.05 taken as significant. In addition, Pearsons correlation was used to determine the correlation between various lab variables and also to find an association by bivariate analysis. Kaplan–Meier analysis was used to get survival curves. All patients who died within 30 days of hospital discharge were excluded from the study. Mortalities after 30 days of hospital discharge were taken into account.

RESULTS

Our study comprised 153 patients of CAP who were followed for median follow-up of 397 days (range 90-720 days). The mean age of patients was 61.31 ± 16.49 years. 99 (62.8%) were males with mean age of 59.53 ± 18.21 years, and 54 patients were females with mean age of 64.59 ± 12.24 years. From a total of 153 patients, 34 (22.22%) patients died at median follow-up of 397 days. We could ascertain the etiology of only 29.1% of patients and in 69.9% etiology was unknown. *Staphylococcus aureus* was the most common organism isolated from survivors (14.1%) as well as nonsurvivors (20.6%). There was no association between particular etiology and survival status as shown in Table 1 and Figure 1. Hypoalbuminemia (*P* = 0.03), increased blood urea nitrogen (BUN) (*P* = 0.00), serum creatinine >1.5 mg/dl, hyperglycemia (>250 mg/dl) (*P* = 0.02), pH <7.35 (*P* = 0.01) were found to be significantly associated with post-discharge mortality as shown in Table 2. Receiver operating characteristic (ROC)

curve of creatinine against death the area under the curve is 0.798 with standard error 0.47, using cut-off value of 1.2 mg/dl we got a sensitivity of 85% and specificity of 77% as shown in Figure 2. As the PSI class of patients increased, the survival decreased with the lowest survival in PSI Class 5 as shown in Figure 3. The ROC curve of PSI class with death as outcome is shown in Figure 4. The area under ROC curve plotted with PSI class against death is 0.734 with a standard error of 0.044 ($P = 0.0001$). Kaplan–Meier curves plotted for PSI class against time; reveal decreasing survival as the PSI class increases. For PSI Classes 3, 4, and 5, we found 24.24%, 27.4%, and 47.8% mortality, respectively, against 0% and 3% mortality in PSI Class 1 and 2, respectively.

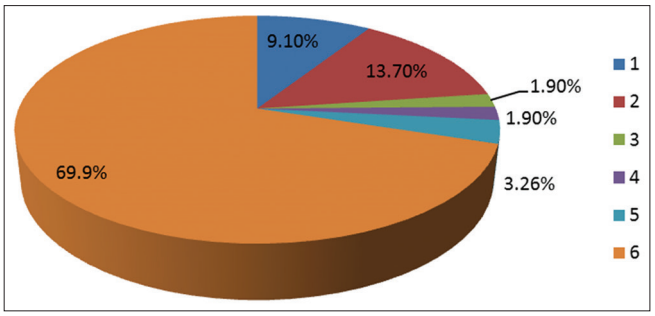


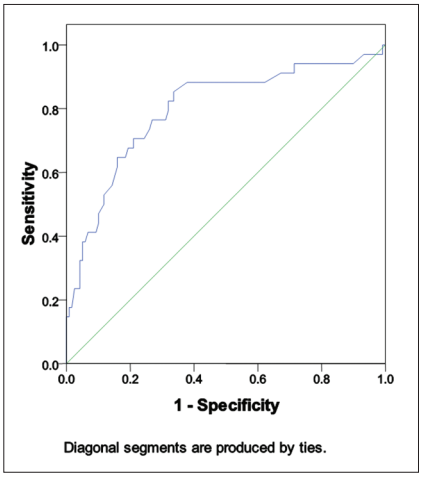
Figure 1: Percentage of different bacteriae in patients with community acquired pneumonia (1) *Streptococcus pneumoniae*, (2) *Staphylococcus aureus*, (3) *Klebseilla pneumoniae*, (4) *Enterococci*, (5) *Pseudomonas*, and (6) etiology not known

DISCUSSION

There is very little data on post hospital survival of patients admitted as CAP from our local population although there are a number of international studies,[1-3,21-23] there is hardly any data available at regional or national level. Little is known what happens to patients admitted as CAP after discharge. We found an appreciable mortality (22.22%) at median follow-up of 397 days post-discharge which highlights the need of close follow-up after

Table 1: Percentage and distribution of microbial etiology

Etiology	Total	Survivors	Nonsurvivors	*P* value
	N=153 (%)	*N*=119 (%)	*N*=34 (%)	
Streptococcus pneumoniae	14 (9.1)	11 (11.11)	3 (8.8)	0.63
Staphylococcus aureus	21 (13.7)	14 (14.1)	7 (20.6)	0.41
Klebseilla pneumoniae	3 (1.9)	2 (2.02)	1 (2.9)	0.79
Enterococci	3 (1.9)	3 (3.03)	0 (0)	0.45
Pseudomonas	5 (3.26)	3 (3.03)	2 (5.8)	0.81
Etiology not known	107 (69.9)	86 (72.2)	21 (61.7)	0.76



Test result variable (s): Serum creatinine

Area	Standard error[a]	Asymptotic significant[b]	Asymptotic 95% CI	
			Lower bound	Upper bound
0.798	0.047	0.000	0.706	0.890

The test result variable (s): Serum creatinine has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased. [a]Under the nonparametric assumption. [b]Null hypothesis: True area=0.5. CI: Confidence interval

Figure 2: Receiver operating characteristic curve for creatinine with death as outcome

Table 2: Descriptives of various laboratory values in survivor and nonsurvivor groups

Variable	Survivor group		Nonsurvivor group		*P* value
	Mean±SD	Range	Mean±SD	Range	
HCO_3	21.7±5.02	9.1-39.5	21.41±6.2	8-31	0.964
pH	7.4±0.07	7.19-7.58	7.36±0.10	7.19-7.58	0.012
Blood glucose	119.4±45.1	70-370	146.1±73.2	72-355	0.153
BUN mg/dl	32.45±23.5	6-106.5	70.5±39.01	9.5-156	0.00
Creatinine mg/dl	1.26±0.83	0.2-5	2.77±1.8	0.3-7.9	0.00
Hemoglobin g/dl	11.39±2.2	6.11-17.80	11.04±3.08	5.5-16.20	0.615
TLC/µl	7900±384	2200-8600	10.36±4.94	1900-22,000	0.192
HCT	35.6±6.01	22-48	34.4±9.21	18-54	0.418
Total protein g/dl	6.63±0.616	5.13-8.60	6.25±0.69	4.90-7.40	0.845
Albumin g/dl	3.06±0.533	1.86-4.5	2.7±0.85	0.2-4.2	0.00

BUN: Blood urea nitrogen, HCT: Hematocrit, TLC: Thin layer chromatography, SD: Standard deviation

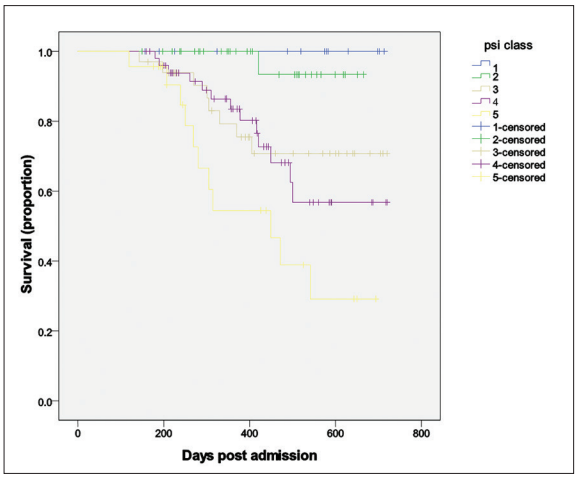
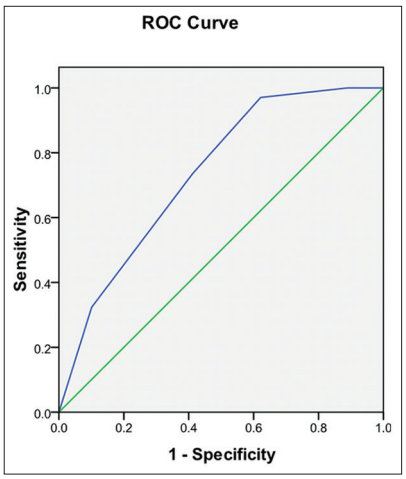


Figure 3: Kaplan–Meier graph showing decreased survival on follow-up with increasing pneumonia severity index class



Area	Standard error[a]	Asymptotic significant[b]	Asymptotic 95% CI	
			Lower bound	Upper bound
0.734	0.044	0.000	0.649	0.820

The test result variable (s): PSI class has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased. [a]Under the nonparametric assumption. [b]Null hypothesis: True area=0.5. CI: Confidence interval, PSI: Pneumonia severity index

Figure 4: Receiver operating characteristic curve for pneumonia severity index class with death as outcome

discharge. There are some studies showing substantial mortality post-discharge (25% at 1 year and 21% at 2.5 years, respectively).[2,8] Factors which we found to be significantly associated with mortality on follow-up included. Hypoalbuminemia (P = 0.03), increased BUN (P = 0.00), serum creatinine >1.5 mg/dl, hyperglycemia (>250 mg/dl) (P = 0.02), pH <7.35 (P = 0.01), bilateral involvement on chest X-ray (P = 0.01), and higher PSI class.

Hypoalbuminemia

Low serum albumin was found to be strongly associated with post-discharge mortality using multivariate analysis (P = 0.03 relative risk [RR] 0.467 and 95% confidence interval [CI] of 0.228-0.957). Bivariate analysis also shows an increase in mortality (P = 0.003) and ICU admission (P = 0.028). Hedlund *et al.*[8] also found an association between serum albumin and post-hospital mortality. Similar finding was confirmed by Woodhead *et al.*,[9] it is said that low albumin in CAP is more because of inflammatory state and less because of nutritional depletion.

BUN

BUN has been found to be a grave sign in CAP, we also found that higher BUN was significantly associated with death even after discharge in CAP, we have found it by univariate analysis (P = 0.000), bivariate analysis (P = 0.00), and also by multivariate analysis (P = 0.000, RR = 1.006, and 95% CI of 1.009-1.030). Patients with high BUN are not only more likely to die on follow-up, but they need ICU admissions than those having low BUN (P = 0.01), but there is no relation between high BUN and rehospitalization. We used the same cut off as that used by Fine *et al.*[4] but our finding is different in the sense that increased BUN is not only associated with increased hospital mortality but also with post-discharge mortality.

Serum Creatinine

Although on multivariate analysis, we could not find significant association between high serum creatinine and mortality, but when used creatinine as a categorical variable with a cut-off value of 1.5 g/dl we have found that patients who were having more than 1.5 g/dl of creatinine on admission were having high mortality (P = 0.00). Also raised serum creatinine associated with ICU admissions (P = 0.01) and death (0.000) by bivariate analysis, when we plot ROC curve of creatinine against death the area under curve is 0.798 with standard error 0.47, using cut-off value of 1.2 mg/dl we got sensitivity of 85% and specificity of 77%. As found by Zalacain *et al.*[21] for post-discharge mortality, we have found that patients increased creatinine level at admission have increased post-discharge mortality.

Hyperglycemia

In our study, we found that there was significant post-discharge mortality in patients who were having blood glucose more than 250 mg/dl on hospital admission (P = 0.02). The risk of increased mortality was also seen by McAlister *et al.*[24] We could not establish a relationship between lower degrees of hyperglycemia (>125 mg/dl) and mortality, since we followed our patients for a maximum of 2 years, the confirmation needs further follow-up.

Arterial Blood Gas (ABG) Analysis

In ABG, we found low pH a predictor of post-discharge mortality. By doing univariate analysis, patients having pH <7.35 we have a remarkable mortality after discharge from the hospital (P = 0.01), bivariate analysis shows

association of low pH with post-hospital mortality ($P = 0.012$) and rehospitalization ($P = 0.002$). Association of PH with mortality was first of all confirmed by Fine *et al.*[4] cut off used by us is same as used by them.

Chest X-ray

We found that patients with bilateral lung involvement are more likely to die during follow-up (univariate analysis $P = 0.03$ by Fisher's exact test). Our findings are in consistence with Leroy *et al.*

PSI Class

We found a positive correlation between high PSI class and subsequent mortality even after hospital discharge, area under ROC curve plotted with PSI class against death is 0.734 with a standard error of 0.044 ($P = 0.0001$). Kaplan–Meier curves plotted for PSI class against time; reveal decreasing survival as the PSI class increases. For PSI Classes 3, 4, and 5, we found 24.24%, 27.4%, and 47.8% mortality, respectively, against 0% and 3% mortality in PSI class 1 and 2, respectively, so we can say that increasing PSI class is not only a predictor of in-hospital mortality but also it can predict post-hospital mortality. Similar findings have been confirmed recently by Johnstone *et al.*[22]

CONCLUSION

There is considerable mortality following discharge of patients admitted with CAP. Hypoalbuminemia, increased BUN, creatinine, blood sugar, low pH and higher PSI class can be used as factors in predicting which patients will have poor outcome after discharge from hospital and hence need a closer follow-up.

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How to cite this article: Sofi FA, Rashid A, Mohammad J, Dhobi GN. Study of Lab Parameters Predicting Post-discharge Mortality after Admission for Community-acquired Pneumonia: A Prospective Tertiary Hospital Care Based Study. Int J Sci Stud 2017;5(4):103-107.

Source of Support: Nil, **Conflict of Interest:** None declared.