Laboratory Abnormalities in Patients With Bacterial Pneumonia*

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Study objectives: This study was undertaken to evaluate the laboratory abnormalities observed in patients with bacterial pneumonia as predictors of the severity of illness.

Design: Retrospective analysis.

Setting: Tertiary care hospital.

Patients and participants: We studied 302 consecutive patients who were admitted to the Long Island Jewish Medical Center from January through December 1993 and treated for bacterial pneumonia. The patients were subdivided into two groups based on their serum phosphorus level either on hospital admission or 4 days before the onset of pneumonia, if this was acquired in-hospital. Hypophosphatemia (group 1) was defined as serum phosphorus level of ≤2.4 mg/dL and normophosphatemia >2.4 mg/dL (group 2). Three hundred randomly selected hospitalized patients treated for conditions other than pneumonia comprised the control group (group 3).

Measurements: Groups 1 and 2 were compared with respect to laboratory data, mortality rate, and duration of hospitalization. The laboratory data of patients in group 3 were compared with those treated for bacterial pneumonia (groups 1 and 2). Stepwise multivariate logistic regression analysis was employed to identify the variables that best predicted the onset of pneumonia.

Results: In groups 1 and 2, a greater (p<0.0001) number of patients (135 of 302 patients with pneumonia, 44.7%) developed hypophosphatemia compared with patients in group 3 (31 of 300 control subjects, 10.3%). Patients with pneumonia (groups 1 and 2) had higher levels (p<0.01) of bicarbonate compared with control subjects. Moreover, patients with pneumonia demonstrated lower levels (p<0.01) of calcium, phosphorus, albumin, cholesterol, and alanine aminotransferase compared with control patients (group 3). Among patients with pneumonia, those with hypophosphatemia (group 1) had significantly lower levels (p<0.05) of potassium, calcium, and albumin compared to those subjects with normophosphatemia (group 2). Furthermore, hypophosphatemic subjects manifested higher levels of glucose (p<0.01) and creatine phosphokinase (p<0.05) compared to their normophosphatemic counterparts. In addition, hypophosphatemic patients experienced a longer duration of hospital stay (hypophosphatemia, 24.6±2.0 days, vs normophosphatemia, 14.1±1.0, p<0.001) and higher (p<0.001) mortality compared to normophosphatemic subjects. The incidence of nosocomial pneumonia was higher (p<0.0001) in hypophosphatemic patients compared to those with normophosphatemia.

Conclusion: We conclude that hypophosphatemia, hypocalcemia, hypokalemia, and hyperalbuminemia may be predictors of the severity of illness in patients admitted to the hospital with bacterial pneumonia.

Key words: bacterial pneumonia; hypophosphatemia; laboratory abnormalities

Pneumonia is the most common life-threatening infectious disease.1 Pleuropulmonary infection remains the fifth most common cause of mortality in the United States, accounting for an estimated 55,000 deaths annually.2 Pneumonia is associated with significant morbidity and prolonged, costly hospitalization, particularly when nosocomial in origin.3

Hypophosphatemia is found in approximately 2 to 3% of patients admitted to hospital with medical illness.4-6 Commonly reported etiologies of hypophosphatemia include alcohol withdrawal/withdrawal, diabetic ketoacidosis, nutritional recovery, alkalotic states, accelerated erythropoiesis, and Gram-negative sepsis.7-13 The triad of hypophosphatemia, hypokalemia, and hypomagnesemia has been de-
scribed in patients in intensive therapy setting, postoperative patients, those with sepsis being treated with aminoglycosides, and oncology patients receiving chemotherapy. Many drugs are known to induce hypophosphatemia, the most common among these being methylprednisolone, epinephrine, albuterol, terbutaline, theophylline, and diethylstilbestrol. Selected cases of atypical pneumonia have been shown to be associated with hypophosphatemia. The mechanism may be through the associated respiratory alkalosis which is known to mediate an intracellular shift of phosphate.

Hypophosphatemia, in addition to its association with conditions listed above, is known to play a role in the impaired chemotaxis, phagocytosis, and bacterial activity of macrophages. There are scanty data on the association of other laboratory abnormalities with the morbidity and mortality in patients with bacterial pneumonia.

**Materials and Methods**

We reviewed the medical records of 353 consecutive patients admitted to Long Island Jewish Medical Center, New Hyde Park, NY, from January 1, 1993 through December 31, 1993, who had bacterial pneumonia as their discharge diagnosis. Of these, 302 patients had documented evidence of bacterial pneumonia, based on chest radiographic evidence of infiltrate with or without positive sputum culture. All of them had at least one full blood chemistry panel drawn at the time of hospital admission. Fifty-one patients were excluded from the study based on one of the following criteria: evidence of respiratory alkalosis on arterial blood gas analysis (pH ≥7.5), chronic alcoholism or alcohol withdrawal, antacid therapy, evidence of disorders like congestive heart failure mimicking pneumonia, or Gram-negative sepsis as all these conditions have been shown to independently cause hypophosphatemia.

Of these 302 patients who satisfied the criteria, the following information was recorded: age, sex, time of occurrence of bacterial pneumonia (on admission or acquired later during hospitalization), number of days of hospital stay, disposition (survival or death), and laboratory tests, including sodium, potassium, chloride, bicarbonate, urea nitrogen, creatinine, glucose, calcium, phosphorus, total protein, albumin, cholesterol, creatine phosphokinase, alanine transaminase, aspartate transaminase, and alkaline phosphatase on admission or before the onset of pneumonia if this developed in the hospital. Hypophosphatemia was defined as a serum phosphorus level ≤2.4 mg/dL. The patients were divided into two groups based on the normal or low serum phosphorus level and clinical and laboratory data were compared between the two groups. To compare the admission electrolyte profile of patients treated for bacterial pneumonia with those of the patients admitted for the treatment of all medical conditions, we also reviewed 300 randomly selected hospital admissions (for conditions other than pneumonia) and recorded the laboratory data as above.

Both univariate and multivariate analyses were employed. Student’s two-tailed t test was used to compare individual variables between groups. Proportions were compared using χ² test with continuity correction or Fisher’s Exact Test when applicable. To identify the best set of variables that predicted the incidence of pneumonia, we carried out stepwise multiple logistic regression analysis. The results were expressed as mean±SEM. A p value <0.05 was considered significant.

**Results**

The total medical admissions to the Long Island Jewish Medical Center over a 3-month period included 7,994 patients. Of these, 640 had documented hypophosphatemia at admission or some time during their hospital stay (8%). In the control group of 300 patients, 31 had documented hypophosphatemia (10.3%). Among 302 patients with a discharge diagnosis of bacterial pneumonia, 135 patients had documented hypophosphatemia (44.7%) (p<0.0001 compared to all hospitalized patients and control group). The sex distribution of the patients among the groups was not significantly different among the groups (control group, female 56.7% vs pneumonia group, female 53.9%). The patients who suffered from hypophosphatemia and pneumonia were significantly older than the control group of medical admissions but not different from the normophosphatemic patients admitted with bacterial pneumonia (hypophosphatemia, 67.5±1.9 years vs control group, 60.7±1.1 years, p<0.001; normophosphatemia, 63.4±1.5 years, p=not significant).

Patients with bacterial pneumonia did not show any difference in sodium, potassium, chloride, glucose, urea nitrogen, creatinine, bilirubin, alkaline phosphatase, creatine phosphokinase, or aspartate transaminase vs the group of patients admitted for conditions other than pneumonia. In contrast, those admitted for bacterial pneumonia demonstrated significantly lower levels of cholesterol, albumin, calcium, phosphorus, and alanine transaminase (Table 1).

Table 2 summarizes the differences in the bio-

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pneumonia</th>
<th>Control</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bicarbonate, mmol/L</td>
<td>25.9 ± 0.3</td>
<td>24.4 ± 0.3</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Calcium, mg/dL</td>
<td>8.8 ± 0.05</td>
<td>8.9 ± 0.05</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Phosphorus, mg/dL</td>
<td>3.1 ± 0.07</td>
<td>3.5 ± 0.06</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Albumin, g/dL</td>
<td>2.9 ± 0.04</td>
<td>3.2 ± 0.05</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cholesterol, mg/dL</td>
<td>156 ± 3</td>
<td>177 ± 4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ALT, U/L</td>
<td>35 ± 4</td>
<td>56 ± 8</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

*Hospital admission blood chemistry results of 302 consecutive patients with the diagnosis of bacterial pneumonia (pneumonia) were compared with the admission blood profile of 300 randomly selected patients admitted for all medical conditions (control) other than pneumonia. Biochemical variables were compared using the Student’s unpaired two-tailed t test. Results are expressed as mean±SEM. ALT=alanine transaminase.
chemical profile of hypophosphatemic subjects with bacterial pneumonia compared to their normophosphatemic counterparts. Hypophosphatemic patients revealed lower levels of potassium, calcium, and albumin compared to their normophosphatemic counterparts. However, hypophosphatemic patients had higher glucose levels. The serum levels of sodium, chloride, urea nitrogen, bicarbonate, creatinine, uric acid, bilirubin, alkaline phosphatase, cholesterol, and aspartate transaminase were not significantly different between the two groups. Moreover, hypophosphatemic patients with pneumonia stayed significantly longer (Fig 1) in the hospital (hypophosphatemia, 24.6±2.1 days vs normophosphatemia, 14.1±1.0; \( p<0.0001 \)). As shown in Figure 2, hypophosphatemic subjects had a higher mortality rate \( (p<0.001) \) than their normophosphatemic counterparts.

The results of the stepwise multiple logistic regression analysis to identify the best predictors of pneumonia are summarized in Table 3. Patients with pneumonia had higher levels of potassium, bicarbonate, and total protein and lower serum levels of phosphorus, calcium, and albumin in comparison with the control group.

Among the patients who experienced hypophosphatemia, 88 patients were admitted with low phosphorus levels and 47 patients had normal phosphorus levels during admission and subsequently developed hypophosphatemia in the hospital. Twenty-two of the 88 patients (25\%) with admission hypophosphatemia and 21 of the 47 (44.7\%) with in-hospital hypophosphatemia died. As represented in Figure 3, the mortality in patients with in-hospital hypophosphatemia was significantly increased in contrast to both those with admission hypophosphatemia as well as those with normophosphatemia (in-hospital hypophosphatemia, 21 of 47 patients died vs admission hypophosphatemia, 22 of 88 patients, \( p=0.0321 \); and vs normophosphatemic patients, 22 of 167 patients; \( p<0.0001 \)). The difference in mortality rate in patients with admission hypophosphatemia was not significantly different vs those with admission normophosphatemia \( (p=0.35) \).

Nosocomial pneumonia is an important problem that contributes significantly to morbidity and mortality in hospitalized patients. Figure 4, which illustrates this problem, shows that 25 of 135 patients with hypophosphatemia and 10 of the 167 patients with normophosphatemia acquired their pneumonia during their hospital stay and this difference was statistically significant \( (p<0.0001) \). Of the 25 patients who acquired their infection after admission to the hospital, 23 had normophosphatemia on admis-

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hypophosphatemia</th>
<th>Normophosphatemia</th>
<th>( p ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potassium, mmol/L</td>
<td>4.2 ± 0.1</td>
<td>4.4 ± 0.1</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Glucose, mg/dL</td>
<td>151 ± 6</td>
<td>129 ± 5</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Calcium, mg/dL</td>
<td>5.3 ± 0.1</td>
<td>5.6 ± 0.1</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Phosphorus, mg/dL</td>
<td>2.5 ± 0.1</td>
<td>3.6 ± 0.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Albumin, g/dL</td>
<td>2.7 ± 0.1</td>
<td>3.0 ± 0.1</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>CPK, U/L</td>
<td>2.40 ± 59</td>
<td>150 ± 15</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

*Biochemical data from 302 consecutive patients who were admitted to the hospital for bacterial pneumonia were analyzed. Of these, 135 developed hypophosphatemia either on admission or during their hospital stay. One hundred sixty-seven patients were normophosphatemic on admission and throughout their stay in hospital. The biochemical profiles of the two groups of patients were compared using the Student’s unpaired two-tailed \( t \) test. The results were expressed as mean±SEM. CPK=creatine phosphokinase.

**Figure 1.** Duration of hospitalization in patients with hypophosphatemia and pneumonia. Bar graph comparing the duration of hospitalization in pneumonia patients who developed hypophosphatemia \( (\text{group 1}) \) and those who did not \( (\text{group 2}) \). Statistical comparison was carried out using Student’s compound \( t \) test. Results were expressed as mean±SEM. The date of death, if applicable, was considered date of discharge from hospital.

**Figure 2.** Mortality in patients with bacterial pneumonia. Bar graph comparing the mortality in hypophosphatemic patients with pneumonia to their normophosphatemic counterparts. \( x^2 \) test was employed for the comparison.
sion and became hypophosphatemic 4 to 6 days prior to the infection episode. Thus, a significant proportion of patients seem to have acquired their hypophosphatemia in the hospital in association with the onset of bacterial pneumonia.

**DISCUSSION**

The elderly ambulatory patient who comes to the emergency department with fever is very likely to have a serious pneumonia and in most instances will require hospitalization.21 Even in young, healthy naval personnel, pneumonia has been found to be the major medical cause of lost workdays.22 Although in western countries pneumonia has been replaced by more chronic pulmonary disorders as the chief cause of respiratory death, it still remains a very important cause of mortality in the United States.2 Hospital-acquired pneumonia is typically much more serious than that acquired in the community,23 in part because of impaired resistance. More importantly, organisms acquired in the hospital tend to be much more pathogenic. These complicated pneumonias are also more difficult to diagnose since the symptoms and signs of the underlying disease (like cardiac failure, malignancy, and acute respiratory distress syndrome) tend to mask the superimposed insult. Nosocomial bacterial infections of the respiratory tract occur in 0.5 to 5.0% of inpatients.24 Although recent studies suggest that most patients who die with hospital-acquired pneumonia have a terminal condition on admission and the infection itself exerts little influence on the prognosis,25,26 it is those patients who did not have a terminal condition on admission whose outcome may be significantly affected.27 The association between nosocomial pneumonia and electrolyte disorders has been rarely studied in the literature.

In our study, we found that 18.5% of hypophosphatemic patients acquired their pneumonia after admission to the hospital compared with 6% of normophosphatemic patients. Moreover, of the 25 patients who developed pneumonia after admission to the hospital, 23 were normophosphatemic on admission and acquired the disorder 4 days before the onset of infection. This observation suggests a possible association between hypophosphatemia and the development of pneumonia and has implications on the management of admitted medical patients. Hypophosphatemia is well known to have adverse effects on many aspects of cell function. The diminished ability of granulocytes for phagocytosis and chemotaxis2 in a low phosphorus milieu has been studied before. It is plausible that these patients

![Table 3—Laboratory Data in Patients With Pneumonia*](image)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Parameter</th>
<th>Estimate</th>
<th>SE</th>
<th>Wald</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phosphorus, mg/dL</td>
<td>0.3812</td>
<td>0.0959</td>
<td>15.794</td>
<td>&lt;0.001</td>
<td></td>
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<tr>
<td>Calcium, mg/dL</td>
<td>0.7705</td>
<td>0.1728</td>
<td>19.8796</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Albumin, g/dL</td>
<td>0.4987</td>
<td>0.1923</td>
<td>6.6430</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td>Potassium, mmol/L</td>
<td>-0.5233</td>
<td>0.1548</td>
<td>11.511</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Bicarbonate, mmol/L</td>
<td>-0.0750</td>
<td>0.0200</td>
<td>14.0797</td>
<td>&lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Total protein, g/dL</td>
<td>-0.3822</td>
<td>0.1539</td>
<td>6.1710</td>
<td>&lt;0.05</td>
<td></td>
</tr>
<tr>
<td>AST, U/L</td>
<td>-0.0055</td>
<td>0.0023</td>
<td>5.5061</td>
<td>&lt;0.05</td>
<td></td>
</tr>
</tbody>
</table>

*Hospital admission chemistry results of the patients with pneumonia were compared to those without pneumonia to identify the variables that best predicted the onset of pneumonia using the stepwise logistic regression analysis. AST = aspartate transaminase.

![Figure 3. Mortality rate in patients with hospital-acquired hypophosphatemia. The mortality in patients with hospital-acquired hypophosphatemia was compared with those who had hypophosphatemia on hospital admission and those with normophosphatemia using a χ² test.](image)

![Figure 4. Incidence of nosocomial pneumonia. The bar diagram represents the percentage of patients with (group 1) and without (group 2) hypophosphatemia and pneumonia who developed nosocomial pneumonia. χ² test was used to compare proportions.](image)
were more prone for infection secondary to their hypophosphatemia. Moreover, the mortality rate among patients with hospital-acquired hypophosphatemia was significantly higher than those admitted with hypophosphatemia (in-hospital hypophosphatemia, 21 of 47 patients died vs admission hypophosphatemia, 22 of 88 patients died; p<0.05). Although we did observe an association between the onset of hypophosphatemia and pneumonia, we did not study the effect of supplementation of phosphorus and its impact on the incidence of pneumonia. Hence, based on our data, we can only speculate on the cause and effect relationship between hypophosphatemia and the onset of respiratory infection.

We investigated the association between typical bacterial pneumonia and electrolyte abnormalities and tried to correlate the findings with the outcome in terms of survival and hospital stay. Although there have been studies looking at the association between hypophosphatemia and survival in surgical patients,28 in all hospitalized patients,29,30 and in patients with respiratory illness,31 to our knowledge, there are none in the literature looking at the association between bacterial respiratory infection and electrolyte disorders, especially in the setting of nosocomial pneumonia. The duration of in-hospital stay and the mortality rate were significantly increased in hypophosphatemic patients compared with normophosphatemic patients. Though these data are, in part, consistent with the data of Fisher et al.,31 there were considerable differences in the inclusion criteria used in the studies. Our sample size was much larger than that of Fisher et al.31 with 302 patients with pneumonia compared to 73. Moreover, the Fisher group did not include diabetics and alcoholics in their hypophosphatemic cohort whereas these patients were included in their control group. Also, Fisher et al.31 did not exclude respiratory alkalosis or antacid consumption in their patient population. In their study, though the hospital stay was prolonged in the hypophosphatemic patients (24±4 days vs 11.3±10 days; p<0.005) compared with their normophosphatemic counterparts, there was no difference in mortality between the two groups. In our study, in addition to increased mortality and prolonged hospital stay, we found that the hypophosphatemic patients had associated electrolyte abnormalities like hypokalemia, hypoalbuminemia, and hypocalcemia.

Iezzoni et al.,32 in their recent retrospective cohort study, compared two clinical methods and three code-based methods to predict the probability of death in patients with all forms of bacterial pneumonia; they found that the clinical data-based methods predicted mortality more consistently than the code-based data. In this study involving 18,016 patients from 105 hospitals with a somewhat comparable age and sex distribution as in our study, serum sodium level of <130 mEq/L, serum albumin level of <2.4 g/dL, and arterial pH <7.34 predicted increased mortality. Our study of patients with bacterial pneumonia followed up in a single hospital was different from Iezzoni et al.32 in that ours was a more homogeneous group. We did not specifically look at the predictors of mortality, though it is interesting that as in our study, a lower serum albumin level predicted mortality.

The combination of alkalosis, hypocalcemia, hypokalemia, and hypophosphatemia in patients admitted to the hospital with bacterial pneumonia signifies that these patients comprised a sicker group of patients. Even among patients with pneumonia, those with hypophosphatemia had a longer duration of hospitalization and higher mortality. Hypophosphatemia was especially ominous when it was acquired in-hospital, suggesting that these patients could have had underlying illnesses that could have contributed to their high risk of death.

**Conclusion**

We conclude that laboratory abnormalities, especially hypophosphatemia, may be a significant risk factor predicting the severity of the underlying illness in hospitalized patients with bacterial pneumonia.

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