Common Laboratory Parameters for Differentiating Between Community-Acquired and Healthcare-Associated Pneumonia

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Background and Objectives: The correct diagnosis of healthcare-associated pneumonia (HCAP) as opposed to community-acquired pneumonia is essential for the selection of a correct empirical antimicrobial approach, reserving the broad-spectrum or highly potent antimicrobial therapies for resistant strains most commonly present in HCAP, whereas treating the less resistant strains, most commonly associated with community and long-term care facility-acquired infections, with a more targeted empirical approach. The standard approach today is to differentiate between the two based on the medical history of the past 90 days prior to admission. Measurable, quantitative assessment may be able to assist in this decision. The objective of this study is to find a measurable method of differentiating between community-acquired and healthcare-associated pneumonias. **Materials and**

Methods: The records of 126 patients admitted with a diagnosis of pneumonia were divided into two groups based on the probable cause of their disease, in accordance with common practice. The routine laboratory work taken upon admittance was analyzed using logistical regression and Student's *t*-test. **Results:** We have found that the red blood cell distribution width and the neutrophil-to-lymphocyte ratio, both routine parameters obtained in a simple blood count, can each assist in differentiating between community-acquired and healthcare-associated pneumonias. **Conclusion:** We have found two statistically significant parameters that may be used as adjuncts to the medical history, chest radiography and other parameters in forming an immediate clinical impression of a patient presenting with pneumonia. *J. Clin. Lab. Anal.* 31:e22016, 2017. © 2016 Wiley Periodicals, Inc.

Key words: community acquired; healthcare associated; neutrophil-to-lymphocyte ratio; pneumonia; red blood cell distribution width

BACKGROUND

Community-Acquired vs. Healthcare-Associated Pneumonia

The various forms of pneumonia are a major cause of morbidity and mortality (1–4). Common practice distinguishes between pneumonia acquired in the community and pneumonia acquired at medical or long-term care facilities, as the former is usually associated with common strains of bacteria, whereas the latter may be associated with resistant strains or other, more violent bacteria (5–8). This distinction has led to the understanding that the empirical antimicrobial treatment used for pneumonia should target the probable

culprit according to the type of infection. Current guidelines define the clinical presentation of pneumonia in patients who have been hospitalized in the past 90 days as healthcare-associated pneumonia (HCAP), and all other forms as community-acquired pneumonia (CAP) (4). Past studies have also demonstrated that residence in a long-term care facility, such as a nursing home, exposes the patient to violent or resistant

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bacterial strains and should be also defined as HCAP (9, 10).

Routine Laboratory Testing Upon Admittance

Upon admission and throughout the hospital-based care of a patient several measurements are routinely taken via a blood sample. These include the following:

C-reactive protein (CRP) is released from hepatocytes due to exposure to proinflammatory cytokines released during acute inflammation, and is considered an acute phase reactant.

Mean platelet volume (MPV) serves as an inflammatory marker and a diagnostic tool as well, for certain viral and bacterial pathogens (11, 12).

Red blood cell distribution width (RDW). Although technically an indication of hematological pathologies, such as anemia and thalassemia, RDW was also found to be a marker of inflammatory processes, mostly chronic (13). The underlying mechanism is yet to be determined. The measured parameter is the variation in erythrocyte size, with a larger variation indicating anisocytosis.

Neutrophil/lymphocyte ratio (NLR) is a simple parameter determined from any blood panel, providing both an indication for the existence of infection, and a clue to its origin (14).

Several studies have attempted to use these parameters for the diagnosis and evaluation of pneumonia (14–19), although without distinction between the two aforementioned types.

Study Objectives

Currently, the treatment plan for patients admitted with a diagnosis of pneumonia is based on a personal history of previous hospitalization and not on quantitative parameters. The purpose of this work is to demonstrate a quantitative method of diagnosis that is able to differentiate between CAP and HCAP.

MATERIALS AND METHODS

This was a retrospective study that was authorized by the institutional ethical review board. The medical records of all patients admitted to the internal medicine department B at Ziv Medical Center, Safed, Israel, with an admission diagnosis of pneumonia between December 2014 and August 2015 were retrieved. This initially resulted in 164 patients, of

which we omitted any patient diagnosed with a malignancy or treated with chemotherapy or dialysis, resulting in a pool of 126 patients. The patient records were examined and each case was designated as either CAP or HCAP, based on the following parameters:

The diagnosis of HCAP was established based on the existence of any of the following:

- (1) Any patient released from hospital care within 90 days prior to admission.
- (2) Any patient who has been a resident of a long-term care facility within 90 days prior to admission.
- (3) Any patient who has received IV antibiotic treatment 30 days prior to admission.
- (4) Any patient who developed pneumonia during hospitalization.
- (5) Any patient with a history of mechanical ventilation and/or clinically significant aspiration within 90 days prior to admission.
- (6) Any patient from whom respiratory tract or blood cultures were taken and the isolated bacteria were of known violent nosocomial strains (e.g., *Pseudomonas aeruginosa*; MRSA).

All other patients were designated as belonging to the CAP category.

The laboratory parameters used for this study were the earliest available, most commonly prior to any administration of medication that could potentially influence the results. The data for CRP, NLR, RDW and MPV for these two groups were analyzed using logistic regression to determine whether a formula may be derived using several or all of these parameters to correctly predict the diagnosis of HCAP or CAP. Calculation of the logistic regression is as follows:

$$\log\left(\frac{P(x)}{1 - P(x)}\right) = \alpha + \beta_1 X_1 + \beta_2 X_2 + \dots \beta_n X_n.$$

Where $\beta_1 X_1, \beta_1 X_2 \dots \beta_1 X_n$ represents the value of a single parameter in all test subjects, $\beta_2 X_1, \beta_2 X_2 \dots \beta_2 X_n$ represents the value of a second parameter in all test subjects, and so on. The sample size n was set as 126. A P -value of 5% (0.05) is considered statistically significant and the statistical power is 80%. Subsequently, each of the aforementioned parameters was individually analyzed using student's t -test to identify a correlation between the two diagnoses and a single parameter. Statistical analysis was performed with the assistance of the BIU faculty of medicine statistical consultant.

RESULTS

Initially, a logistic regression test was performed to ascertain whether a certain combination of laboratory values could reach the correct diagnosis of pneumonia. This showed that no combination of these values assists in the diagnosis of HCAP vs. CAP. It did show an indication for the predictive values of NLR and RDW as solitary parameters, used individually. We then attempted to apply a logarithmic transformation to the laboratory values, recalculating the logistic regression test using the function $\text{Log}_{10}(X)$, where X represents the aforementioned laboratory values. This did not prove to assist, and we therefore concluded that a formula using some or all of the values of NLR, RDW, MPV, and CRP or their logarithmic transformations cannot distinguish between CAP and HCAP. We subsequently attempted to analyze the predictive ability of each parameter on its own, focusing mainly on RDW and NLR, as their predictive ability was previously indicated. The data for the neutrophil-to-lymphocyte ratio (NLR) are presented in Figure 1. This showed that the average NLR value for patients with CAP is 9.39, whereas its value for patients diagnosed with HCAP is 14.37. A student's t -test was performed on these data and the differences were found to be significant with a P -value of <0.01 . It has also been demonstrated that with a 95% confidence interval it may be said that any NLR value higher than 11.206 is predictive of HCAP, although only patients with an NLR lower than 9.78 may be said to not have HCAP, with a 95% confidence interval. The data for RDW are presented in Figure 2. This showed that the average RDW value for patients diagnosed with CAP was 14.098%, whereas the average RDW value for patients diagnosed with HCAP was 16%. A student's t -test was performed and the differences were found to be

Fig. 1. Average neutrophil / lymphocyte ratio values for patients diagnosed with CAP vs. patients diagnosed with HCAP. Error bars represent SE.

RBC distribution width

Fig. 2. Average red blood cell distribution width values for patients diagnosed with community-acquired pneumonia vs. patients diagnosed with healthcare-associated pneumonia. Error bars represent SE.

significant with a P -value of <0.01 . It has also been demonstrated that with a 95% confidence interval it may be said that any RDW value above 15.3% is indicative of HCAP and any case in which the RDW is lower than 14.392% may be safely assumed not to have HCAP. Data for CRP and MPV did not show any statistically significant difference between the two groups.

DISCUSSION

Our results demonstrate an ability to predict whether pneumonia is community acquired or healthcare associated based on routine parameters derived from a simple and inexpensive complete blood count taken routinely upon any admission to the hospital, regardless of the patient's medical history or clinical signs and symptoms. This may be of significant benefit especially when an adequate history cannot be obtained, or when a targeted antimicrobial approach is deemed necessary, such as when broad-spectrum antibiotics are contraindicated. Using this method, results can be obtained within minutes, as opposed to cultures which may take days to grow.

There are possible limitations to this study. Patients suffering from HCAP may present with additional nosocomial infections, affecting and altering the parameters presented above. In addition, as a rise in the neutrophil count occurs most commonly with bacterial infections, it is not surprising that as the severity of the infection increases, so does the NLR, regardless of the strain or virulence of the infecting pathogen. It is also possible that due to the clinical severity of those patients affected with HCAP, a prior use of medication (such as inhaled corticosteroids) is more likely and this may have altered the results. In conclusion, we have found two statistically significant parameters

that may be used as adjuncts to the medical history, chest radiography and other parameters in forming an immediate clinical impression of a patient presenting with pneumonia, prior to the successful growth of cultures.

AUTHORS' CONTRIBUTIONS

RF: have performed all the study conception and design, acquisition of data, analysis and interpretation of data, writing the manuscript. PG: has been involved in drafting the manuscript and revising it. JB: has been involved in collecting data and analysis. RKF: participated in the design of the study and performed the statistical analysis.

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