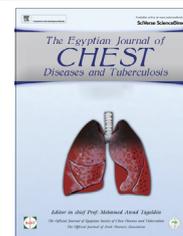




The Egyptian Society of Chest Diseases and Tuberculosis
Egyptian Journal of Chest Diseases and Tuberculosis

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ORIGINAL ARTICLE

Thrombocytosis at time of hospitalization is a reliable indicator for severity of CAP patients in ICU

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Received 5 May 2012; accepted 15 May 2012

Available online 31 January 2013

KEYWORDS

Community-acquired pneumonia;
 PSI;
 CURB-65 score;
 Thrombocytosis;
 Leucocytosis

Abstract *Background:* Clinicians have always evaluated the degree of leukocytosis in patients with pneumonia as an indication of systemic inflammatory response and severity of disease. But platelets have been increasingly recognized as inflammatory cells with an important role in host defenses.

Objective: To evaluate if abnormal platelet count in hospitalized patients with CAP was associated with severity of CAP comparing it with abnormal leucocytes' count.

Methods: The study enrolled 66 patients with community acquired pneumonia admitted to respiratory ICU of Ain Shams University and Ain Shams University specialized hospitals. Data were collected from each patient including demographic data, clinical findings, comorbidities, laboratory data, arterial blood gas results, chest radiographic findings; pneumonia severity index (PSI) and CURB-65 were calculated. Simple correlations between variables were examined by calculating Pearson's product correlation coefficient. Four models of multiple linear regression analysis was performed to study the simultaneous effects of the different data variables on PSI, CURB-65 score, need for mechanical ventilation and length of stay in ICU as dependent variables respectively indicating pneumonia severity.

Results: There were significant correlations between the following: personal data, clinical findings, arterial blood gas findings, laboratory results, radiological findings and data of severity which are (PSI, PSI class, CURB-65 score, length of stay in ICU, mechanical ventilation) ($p < 0.001$). Thrombocytosis was strongly associated with CAP severity parameters and was more significant than abnormal leucocytic count in predicting the severity of CAP as studied on their effect

Abbreviations: CAP, community-acquired pneumonia; PSI, pneumonia severity index; CURB-65, confusion, urea ≥ 7 mmol/L, respiratory rate ≥ 30 breaths/min, blood pressure ≤ 90 mm Hg systolic or ≤ 60 mm Hg diastolic, age ≥ 65 years.

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Peer review under responsibility of The Egyptian Society of Chest Diseases and Tuberculosis.



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on PSI, CURB-65 score and need for mechanical ventilation; while leucocytosis was more significant in predicting the length of stay in ICU than thrombocytosis.

Conclusion: Thrombocytosis can be used as a marker of severity in patients with community-acquired pneumonia better than leucocytes' count.

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Introduction

Community-acquired pneumonia (CAP) continues to be associated with significant morbidity and mortality, is ranked together with influenza as the eighth leading cause of death in the United States [1]. Physicians continue to be either conservative or overestimating the risk of death in patients with pneumonia, and therefore affecting the decision to hospitalize many patients. Severity scores provide pivotal direction for the management of community-acquired pneumonia helping guide decisions such as the appropriate venue for care, diagnostic strategies, and antibiotic therapies. Fine and his colleagues [2] have provided us with a validated evidence-based tool and a most popular severity scores, the pneumonia severity index (PSI) which is specific for predicting mortality, besides the British Thoracic Society's CURB-65 [3] (Confusion, urea ≥ 7 mmol/L, respiratory rate ≥ 30 breaths/min, blood pressure ≤ 90 mm Hg systolic or ≤ 60 mm Hg diastolic, age ≥ 65 years) are accurate for predicting pneumonia-related mortality. These tools are simple to apply and highly useful in practice, and have been widely adopted [4,5].

No matter how simple or validated a tool may be, many physicians find any scoring system cumbersome and would prefer a single surrogate blood test that would allow them to predict outcomes and to stratify risk in patients [6].

Previously, Clinicians have always evaluated the degree of leukocytosis in patients with pneumonia as an indication of systemic inflammatory response and severity of disease. But Platelets have been increasingly recognized as an important component of innate and adaptive immunity. Platelet response in antimicrobial host defense is similar, in many ways, to the leukocyte response.

Both cell types contain antimicrobial peptides that act against a broad range of pathogens that contributes to limiting the infection [7]. Therefore, Thrombocytopenia is also a recognized marker of poor outcomes in patients with pneumonia, due to the association of low platelet counts with disseminated intravascular coagulation and severe sepsis [8]. However, to our knowledge scanty studies investigated the association between thrombocytosis and clinical outcomes in adult patients with CAP [9]. Therefore, considering that platelets play a crucial role in antimicrobial host defenses and the coagulation system, the primary objective of this study was to investigate the association of an abnormal platelet count as an important marker to assess severity of disease in patients with CAP versus the usual counting on the total leukocyte count.

Subjects and methods

Patients and study design

The study was conducted on 66 patients, all had community acquired pneumonia and all were admitted to respiratory ICU of Ain Shams University and Ain Shams University

specialized hospitals. Data were collected from each patient including demographic data, clinical findings, comorbidities, laboratory data, arterial blood gas results, chest radiographic findings, the collected data were used to calculate the patient's pneumonia severity using the pneumonia severity index (PSI) and CURB-65 (confusion, urea, respiratory rate, blood pressure, age ≥ 65 years). There were no exclusion criteria.

Definitions

CAP was defined as the presence of a new pulmonary infiltrate on chest radiograph at the time of hospitalization associated with at least one of the following: (1) new or increased cough, (2) an abnormal temperature (< 35.6 °C or > 37.8 °C) and (3) an abnormal serum leukocyte count (leukocytosis, left shift, or leucopenia defined by local laboratory values). Hypotension as defined as a systolic blood pressure ≤ 90 mm Hg or diastolic blood pressure ≤ 60 mm Hg. Alteration of gas exchange was defined as $\text{PaO}_2 < 60$ mm Hg or $\text{PaO}_2/\text{FIO}_2 < 300$ or O_2 saturation $< 90\%$. Thrombocytopenia and thrombocytosis were defined as platelet counts $< 150,000/\text{L}$ or $> 400,000/\text{L}$, respectively. Significant leucopenia and leukocytosis were defined as WBC counts of $< 4,000$ and $> 11,000$, respectively [9].

Data analysis

Simple correlations between variables were examined by calculating Pearson's product correlation coefficient. Multiple linear regression analysis was performed to study the simultaneous effects of the different data variables on each parameter indicating pneumonia severity as a dependent variable. Data are presented as mean \pm SD for continuous variables or frequency (percentage %) for categorical variables, $P < 0.05$ was considered significant. Analysis was performed using the statistical software (SPSS version 17; SPSS, Inc., Chicago, IL, USA).

Results

Sixty-six patients with community acquired pneumonia were recruited from the respiratory ICU of Ain Shams University hospital and Ain Shams University Specialized hospital. The patient characteristic data are described in Table 1.

Data presented as mean \pm SD or frequency (percentage); SBP, systolic blood pressure; DBP, diastolic blood pressure; ABG, arterial blood gases; ALB, albumin; HCT, hematocrit value; TLC, total leukocytic count; PSI, pneumonia severity index; MV, mechanical ventilation; CURB-65: confusion, urea, respiratory rate, blood pressure, age > 65 years.

Correlations of different data with the parameters indicating severity on admission (PSI, PSI class, CURB-65 score, length of stay in ICU, mechanical ventilation) were done using Pearson's product correlation. There were significant correlations between the following: personal data (age, sex, smoking

Age (mean \pm SD)		54.32 \pm 16.78
Sex	Male (%)	36 (54.5)
	Female (%)	30 (45.5)
Smoking	Smoker (%)	39 (59.1)
	Non (%)	27 (40.9)
Length of stay in ICU, <i>d</i> (mean \pm SD)	14.11 \pm 6.18	
<i>Clinical data findings:</i>		
Conscious level	Conscious (%)	30 (45.5)
	Disturbed (%)	36 (54.5)
Temperature (C°) (mean \pm SD)		39.1 \pm 0.93
Respiratory rate (/min) (mean \pm SD)		31 \pm 5
Heart rate (/min) (mean \pm SD)		118 \pm 19
SBP, mmHg (mean \pm SD)		103 \pm 15
DBP, mmHg (mean \pm SD)		66 \pm 8
<i>Severity on ICU admission:</i>		
Mechanical ventilation	No MV (%)	33 (50)
	MV (%)	33 (50)
PSI (mean \pm SD)		149.06 \pm 73.97
PSI risk class (%)	I (%)	9 (13.6)
	II (%)	5 (7.6)
	III (%)	4 (6.1)
	IV (%)	15 (22.7)
	V (%)	33 (50)
	VI (%)	14 (21.2)
CURB-65 score (%)	0 (%)	14 (21.2)
	1 (%)	6 (9.1)
	2 (%)	10 (15.2)
	3 (%)	6 (9.1)
	4 (%)	21 (31.8)
	5 (%)	9 (13.6)
<i>Arterial blood gas results:</i>		
PH (mean \pm SD)		7.40 \pm 0.06
PO ₂ , mmHg (mean \pm SD)		51.78 \pm 13.4
PO ₂ /FIO ₂ ratio (mean \pm SD)		246.8 \pm 64.02
<i>Laboratory results:</i>		
ALB, mg/dl		3.3 \pm 0.6
BUN, mg/dl		31 \pm 9
CREAT, mg/dl		1.1 \pm 0.4
NA, mg/dl		131 \pm 5.8
HCT, % (%)		31.2 \pm 5.8
TLC, cell/ μ l (mean \pm SD)		16386.36 \pm 5752.4
Platelets, cell/ μ l (mean \pm SD)		402893.94 \pm 175456
<i>Radiological findings:</i>		
Distribution	Localized (%)	33 (50)
	Multilobar (%)	33 (50)
Side	Right (%)	18 (27.3)
	Left (%)	24 (36.4)
	Bilateral (%)	24 (36.4)
		24 (36.4)
Pleural effusion	Yes (%)	27 (40.9)
	No (%)	39 (59.1)
Loculation	Yes (%)	51 (77.3)
	No (%)	15 (22.7)

status), clinical findings (conscious level, temperature, respiratory rate, heart rate, systolic and diastolic blood pressure), arterial blood gas findings (PH, PO₂, PO₂/FIO₂ ratio), laboratory results (BUN, creatinine, Na, hematocrit, total leucocytic count, platelet count), radiological findings (distribution in X-ray, side, loculation of the effusion) and data of severity which are (PSI, PSI class, CURB-65 score, length of stay in

ICU, mechanical ventilation) ($p < 0.001$). There were no significant correlation between the presence of pleural effusion and the parameters of severity of pneumonia, while albumin level was only significantly correlated with PSI and PSI class ($p < 0.05$).

The predictors for severity of community acquired pneumonia on admission to ICU were examined by using multiple

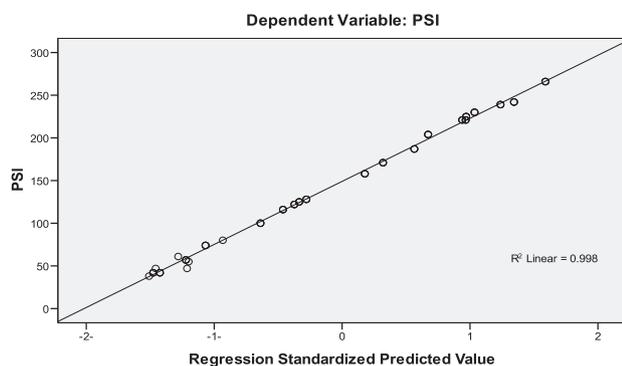


Figure 1 Multiple linear regression model on PSI, independent variables are the personal, clinical, laboratory, arterial blood gas and radiology data. The model is significant ($F = 857.99$, $p = 0.000$) with coefficient of determination of 99.7%.

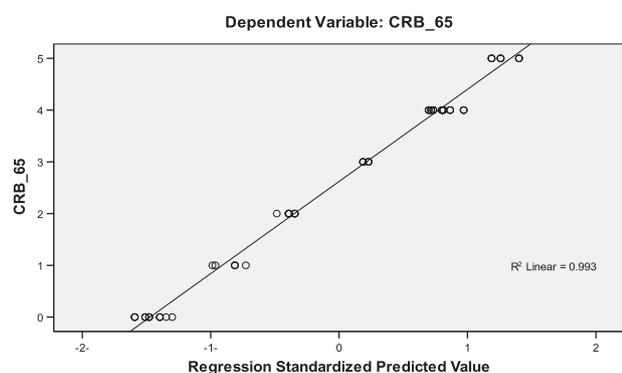


Figure 2 Multiple linear regression model on CURB-65 score, independent variables are the personal, clinical, laboratory, arterial blood gas and radiology data. The model is significant ($F = 273.56$, $p = 0.000$) with coefficient of determination of 99%.

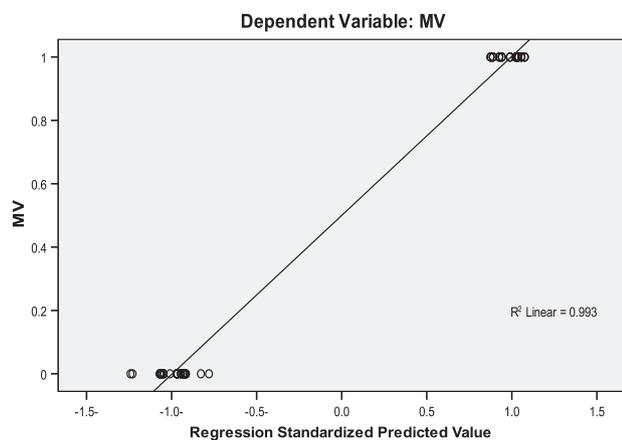


Figure 3 Multiple linear regression model on the need for mechanical ventilation, independent variables are the personal, clinical, laboratory, arterial blood gas and radiology data. The model is significant ($F = 290.18$, $p = 0.000$) with coefficient of determination of 99%.

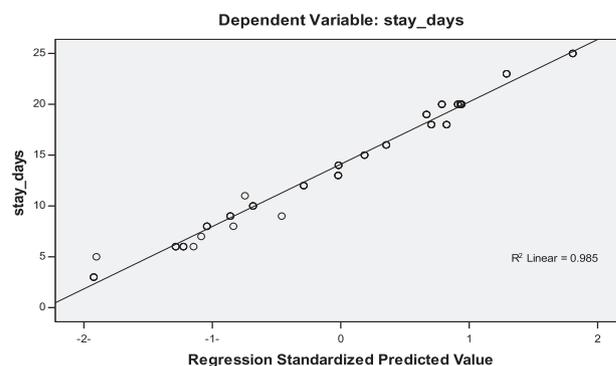


Figure 4 Multiple linear regression model on the length of stay in ICU, independent variables are the personal, clinical, laboratory, arterial blood gas and radiology data. The model is significant ($F = 123.44$, $p = 0.000$) with coefficient of determination of 97.7%.

linear regression models with a parameter for severity of pneumonia as a dependent factor for each model; and including all the personal, clinical, laboratory, arterial blood gas and radiology data as independent variables.

The first multiple linear regression model used PSI as a dependent variable, it was significant ($F = 857.99$, $p = 0.000$) and accounts for 99.7% of estimation of PSI. The most powerful predictor was altered conscious level followed by platelet count, while total leucocytic count had no significant effect ($p = 0.137$); this is presented in Fig. 1.

The second linear regression model used CURB-65 score as a dependent variable, it was significant ($F = 273.56$, $p = 0.000$) and accounts for 99% of prediction of CURB-65 score. The most powerful predictor was platelet count while TLC was very less significant. It is illustrated in Fig. 2.

The third linear regression model included mechanical ventilation as a dependent variable, the model was significant ($F = 290.18$, $p = 0.000$) and it explains 99% of the need for mechanical ventilation; platelet count was the most significant independent factor and TLC was very less significant in prediction of the need for mechanical ventilation; the model is presented in Fig. 3.

The last regression model used the length of stay in ICU as a dependent variable, this model is significant ($F = 123.44$, $p = 0.000$) and it accounts for 97.7% of prediction of the length of stay in ICU, in contrast to the previous models, platelet count has no significant effect while the TLC was one of the most powerful predictors. The model is shown in Fig. 4.

Discussion

Accurate assessment the severity of pneumonia is the key to managing patients with CAP appropriately. In this study, conducted in a cohort of patients hospitalized in ICU with CAP, estimation of the PSI and CURB-65 scores were performed, regarding that several previous studies have shown that the PSI and CURB-65 appropriately stratify severity, the need for mechanical ventilation and the duration of hospital stay [4,10].

In our study the predictors for severity of CAP on admission to ICU was examined by using multiple linear regression

models. In the first model which used PSI as a dependent variable; the most powerful predictor was altered conscious level followed by platelet count, while total leucocytes' count had no significant effect ($p > 0.05$), these results agree with the previous study which indicated that thrombocytopenia and thrombocytosis are significantly associated with mortality in patients with CAP, therefore at time of hospitalization, abnormalities in platelet count are better predictors of clinical outcomes in patients with CAP when compared with abnormalities in leukocyte count. Besides, in the multivariable logistic regression model, mortality in hospitalized patients with CAP is associated with severity of disease but it is also independently associated with elevated platelet count [9].

The second model used CURB-65 score as a dependent variable; the most powerful predictor was platelet count while TLC was very less significant. Similarly two prior studies, both in pediatric patients, reported an association between thrombocytosis and poor outcomes in patients with CAP [11,12].

The third linear regression model included mechanical ventilation as a dependent variable, platelet count was the most significant independent factor and TLC was very less significant in prediction of the need for mechanical ventilation.

Two possible pathophysiological mechanisms may explain our study findings, platelets are important inflammatory cells that can undergo chemotaxis and are able to release numerous proinflammatory molecules [13]. In patients with CAP there is an association between levels of inflammatory cytokines and severity of disease [14]. It can be theorized that thrombocytosis may favor an exaggerated systemic inflammatory response that, in turn, produces poor outcomes in patients with CAP. Besides this mechanism of platelet induced systemic inflammation, another possible mechanism is platelet-induced thrombus formation which is a risk factor for pulmonary thromboembolism and acute myocardial infarction and cerebrovascular stroke that also may add on risk of mortality [9,15].

In contrast to the previous models, the model used the length of stay in ICU as a dependent variable; in this model platelet count has no significant effect while the TLC was one of the most powerful predictors. These results found as regards duration of hospital stay are affected by other factors, such as the causal microorganism, comorbidities and treatment-related factors which are not included in our study. [16] Therefore, it must be noted that the initial severity of CAP is an only one factor predicting treatment failure which in turn increase duration of hospital stay.

In summary, the initial assessment of a patient with pneumonia, it is mandatory to consider thrombocytosis as a predictive factor for severity of pneumonia. Moreover, when evaluating a complete blood count report in patients with CAP, platelet count may be more informative for predicting patient poor outcomes than the more commonly used leukocyte count.

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