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Platelet count as a predictor of outcome of hospitalized patients with community-acquired pneumonia at Zagazig University Hospitals, Egypt

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Abstract

Background: Platelets play an essential role in both coagulation system and the host immune defenses against infection including community-acquired pneumonia (CAP). This work aimed to study the possibility of using platelet count as an additional criterion to predict the outcome of hospitalized patients with CAP.

Results: This prospective cohort study included 250 patients hospitalized with CAP. According to platelet count at admission, 15 (6%) patients showed thrombocytopenia (group I) and 202 (80.8%) showed normal platelet count (group II), while 33 (13.2%) patients showed thrombocytosis (group III). CAP patients with thrombocytosis had more significant respiratory complications including lung abscess ($p = 0.02$), empyema ($p < 0.001$), and pleural effusion ($p = 0.01$). Severe sepsis and septic shock were significantly encountered among CAP patients with thrombocytopenia ($p = 0.02$ and 0.03, respectively). CAP patients with thrombocytopenia significantly needed mechanical ventilation either invasive ($p = 0.017$) or even non-invasive ($p = 0.047$). Both CAP patients with thrombocytopenia or thrombocytosis had significant 30 days readmission ($p = 0.034$) and significant 30 days mortality ($p = 0.016$) when compared to CAP patients with normal platelet count. Both thrombocytopenia ($p = 0.012$) and thrombocytosis ($p = 0.029$) were independent predictors of 30 days mortality among hospitalized patients with CAP.

Conclusions: Both thrombocytosis and thrombocytopenia are linked to adverse outcomes among hospitalized patients with CAP.

Keywords: Community-acquired pneumonia, Thrombocytopenia, Thrombocytosis

Background

Community-acquired pneumonia (CAP) is both a common and probably serious disease. It is linked to increasing mortality, especially in patients with comorbidities and in the elderly [1].

Platelets are considered a cornerstone in the process of hemostasis. Also, they are now well known to be an essential part of the immune response to various infectious agents [2]. Platelets are essential inflammatory cells that can be recruited to the site of inflammation and have the ability to release multiple proinflammatory cytokines [3].

Thrombocytopenia is a well-known marker of adverse outcome in patients diagnosed with pneumonia, as decreased platelet count is linked to severe intravascular coagulation and severe sepsis [4]. On the other hand, thrombocytosis has been recognized as a normal response to infection, but not as a marker of an unfavorable outcome. CAP patients with thrombocytopenia or thrombocytosis may show different clinical pictures, inflammatory biomarkers, and mortality figures than those with normal platelet count [5]. So, we conducted this work to study the possibility of using platelet count as

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an additional criterion to predict the outcome of hospitalized patients with CAP.

Methods

Study design and setting

This prospective cohort study was carried out at Internal Medicine and Chest Departments and ICUs of Zagazig University Hospitals, from December 2013 to December 2014.

Patients

This study included 250 consecutive patients hospitalized with CAP. CAP was diagnosed if chest radiograph showed a new or progressive lung infiltrate, plus at least two of the following: fever more than 38.5 °C, cough, purulent sputum production, or leukocytosis more than 10,000/cmm. Those parameters had to be found ≤ 48 h of admission [4]. Patients with age less than 18 years, immunosuppression, neoplastic disorder, active tuberculosis, or hematologic disease were excluded. This research was approved by the Ethics Committee of Zagazig, Faculty of Medicine. An informed written consent was collected from all participants. Identification of patients remained anonymous throughout the study.

Methods

All participants underwent the following:

1) Medical history taking.
2) Clinical examination.
3) Plain chest radiograph.
4) Arterial blood gases (ABGs).
5) Routine laboratory investigations:

- Complete blood count (CBC).
- Liver and kidney function tests.

6) Severity assessment using CURB-65 score on admission: [confusion, blood urea nitrogen, respiratory rate (RR), blood pressure plus age equal or more than 65 years]. All included patients had a total score > 1. Patients with a score of 0 or 1 were considered for home treatment [6].
7) Criteria of ICU admission: ICU admission was considered if the patient had one major or three minor criteria according to IDSA/ATS guidelines [4].
8) Classification of patients: patients were classified according to their platelet count at presentation into three groups: group I, patients with thrombocytopenia (platelet count < 100000 cells/mm3); group II, patients with normal platelet count; and group III, patients with thrombocytosis (platelet count ≥ 400,000 cells/mm3).
9) Assessment of duration of hospital stay and occurrence of complication(s), e.g., lung abscess, sepsis, severe sepsis, septic shock, pleural effusion, complicated parapneumonic effusion, empyema, or need for mechanical ventilation (either invasive or noninvasive). *Empyema* was diagnosed if frank pus retrieved from the pleural cavity, positive Gram stain, or an organism was cultured from pleural fluid. *Complicated parapneumonic effusion* was diagnosed if pleural fluid analysis showed at least two of the following: glucose equal or less than 40 mg/dl, lactate dehydrogenase equal or more than 1000 u/L, pH ≤ 7.2, and WBC count equal or more than 10,000 cells/cmm [7]. *Pleural effusion* the presence of pleural fluid was confirmed by chest radiograph and ultrasonography [8]. *Sepsis* was defined as infection plus systemic manifestations of infection [9]. *Severe sepsis* was defined as sepsis plus sepsis-induced organ dysfunction or tissue hypoperfusion. *Septic shock* was defined as severe sepsis plus hypotension not reversed with fluid resuscitation [10].
10) Assessment of final outcome, which was either mortality or readmission within 30 days after admission.

Statistical analysis

All data were checked and analyzed using Epi-Info TM version 6 (available at https://wwwn.cdc.gov/epiinfo/html/ei6_downloads.htm) and Statistical Package for Social Science (SPSS version 19; SPSS, Inc., Chicago, IL, USA). Results of this work were analyzed and presented as number and percentage or mean ± standard deviation (SD). Chi-square, analysis of variance (ANOVA), and multivariable logistic regression models were used for comparisons between the groups' data. A P-value < 0.05 was considered significant and p value < 0.001 was considered highly significant.

Results

This study included 250 hospitalized patients with CAP, their ages ranged from 20 to 85 with a mean age of 59.1 ± 13.9 years. There were 157 (62.8%) males and 93(37.2%) females. Fifteen (6%) patients showed thrombocytopenia (group I) and 202 (80.8%) showed normal platelet count (group II), while 33 (13.2%) patients showed thrombocytosis (group III). CAP patients with thrombocytopenia were significantly older than those with thrombocytosis and those with normal platelet count (p < 0.001). There was no statistically significant difference among all studied groups as regard sex, smoking status, and intake of antiplatelet therapy. Also, chronic heart (p = 0.001) and renal

Table 1 Sociodemographic data of all studied patients

Parameter	Group			Total (n = 250)	χ^2	p value
	Group I (n = 15)	Group II (n = 202)	Group III (n = 33)			
Age ± SD, years	73 ± 9.5	59 ± 19	54.2 ± 12.6	59.1 ± 13.9	14.56*	< 0.001[a]
Male	8 (63.3%)	132 (65.3%)	17 (51.5%)	157 (62.8%)	2.93	0.23
Female	7 (46.7%)	70 (34.7%)	16 (50%)	93 (37.2%)		
Non-smoker	8 (53.3%)	111 (55.0%)	24 (72.7%)	143 (57.2%)	3.75	0.15
Smoker	7 (46.7%)	91 (45.0%)	9 (27.3%)	107 (42.8%)		
Antiplatelet therapy	3 (20.0%)	23 (11.4%)	3 (9.1%)	29 (11.6%)	1.24	0.53
Comorbidities						
Respiratory	4 (26.7%)	89 (44.1%)	15 (45.5%)	108 (43.2%)	1.8	0.4
Cardiac	8 (53.3%)	33 (16.3%)	4 (12.1%)	45 (18.0%)	13.1	0.001[a]
Diabetes mellitus	2 (13.3%)	34 (16.8%)	5 (15.2%)	43 (17.2%)	0.16	0.91
Hepatic	4 (26.7%)	13 (5.9%)	2 (6.1%)	18 (7.2%)	6.2	0.04[a]
Renal	2 (13.3%)	9 (4.5%)	1 (3.0%)	12 (4.8%)	2.66	0.26

Group I, thrombocytopenia; group II, normal platelet count; group III, thrombocytosis
*One-way ANOVA is used
[a]Difference between group I and other groups

(p = 04) comorbidities were more frequent among patients with thrombocytopenia. Sociodemographic data of all studied patients are shown in Table 1.

Table 2 shows that CAP patients with thrombocytopenia had lower PaO_2/FIO_2 (p = 0.005), more prolonged prothrombin time (p < 0.001), higher serum urea (p < 0.001), and lower serum albumin levels (p < 0.001) when compared to patients with thrombocytosis or patients with normal platelet count, while CAP patients with thrombocytosis had higher leucocytic count (p < 0.001) when compared to patients of the other two groups.

Table 3 shows that the CURB-65 severity score (on admission) was significantly higher among CAP patients with thrombocytopenia when compared to those patients with normal platelet count or those with thrombocytosis (p = 0.03).

Table 4 shows that CAP patients with thrombocytosis had more significant respiratory complications including; lung abscess (p = 0.02), empyema (p < 0.001), and pleural effusion (p = 0.01), when compared to CAP patients with thrombocytopenia or CAP patients with normal platelet count.

Table 5 shows that severe sepsis and septic shock were significantly encountered among CAP patients with thrombocytopenia (p = 0.02 and 0.03, respectively), when compared to CAP patients with normal platelet count or CAP patients with thrombocytosis.

Table 6 shows that the need for ICU admission was significantly higher among CAP patients with thrombocytopenia (53.3%), when compared to CAP patients with thrombocytosis (12.1%) or CAP patients with normal platelet count (8.4%) (p < 0.001), while length of hospital stay did not differ among all groups.

Table 2 ABG_s and laboratory parameters on admission among all studied groups

Parameter	Group			One-way ANOVA	p value
	Group I (n = 15)	Group II (n = 202)	Group III (n = 33)		
Arterial pH	7.39 ± 0.07	7.43 ± 0.07	7.43 ± 0.06	2.832	0.06
PaO_2, mmHg	58.6 ± 14.1	63.6 ± 12.2	61.3 ± 9.8	1.586	0.21
PaO_2/FIO_2	305.3 ± 50.6	345.9 ± 38.0	335.8 ± 41.4	5.474	0.005a
WBCs × $10^3/mm^3$	10.79 ± 2.8	14.47 ± 3.9	17.40 ± 5.3	14.137	< 0.001[b]
Prothrombin time, s	15.3 ± 2.1	12.5 ± 1	11.6 ± 1.2	15.091	< 0.001a
Serum urea, mg/dl	39.7 ± 11.4	27.1 ± 7.7	22.6 ± 6.7	9.432	< 0.001a
Serum albumin, g/dl	2.9 ± 0.5	3.2 ± 0.4	3.2 ± 0.5	4.183	0.016a

Group I, thrombocytopenia; group II, normal platelet count; group III, thrombocytosis
ABG_S arterial blood gases, *PaO_2* partial arterial oxygen pressure, *FIO_2* fraction of inspired oxygen, *WBCS* white blood cells
[a]Difference between group I and other groups
[b]Difference between group III and other groups

Table 3 CURB-65 score on admission among all studied groups

CURB-65	Group			Total (n = 250)	χ^2	p value
	Group I (n = 15)	Group II (n = 202)	Group III (n = 33)			
Score 2–3	2 (13.3%)	68 (33.7%)	12(36.4%)	82 (32.8%)	6.9	0.03[a]
Score 4–5	13 (86.7%)	134(66.3%)	21(63.6%)	168(77.2%)		

Group I, thrombocytopenia; group II, normal platelet count; group III, thrombocytosis
[a]Difference between group I and other groups

Table 7 shows that CAP patients with thrombocytopenia significantly needed mechanical ventilation either invasive (p = 0.017) or even non-invasive (p = 0.047), when compared to CAP patients both with thrombocytosis or with normal platelet count.

Table 8 shows that both CAP patients with thrombocytopenia and CAP patients with thrombocytosis had significant 30 days readmission (p = 0.034) and significant 30 days mortality (p = 0.016) when compared to CAP patients with normal platelet count.

Table 9 shows predictors of 30 days mortality among hospitalized patients with CAP in the current study, using multivariate regression analysis model. Mortality was independently associated with septic shock (p < 0.001), older age more than 65 years (p = 0.002), confusion at admission (p = 0.006), thrombocytopenia (p = 0.012), PaO2/FIO2 < 200 mmHg (p = 0.017), and thrombocytosis (p = 0.029).

Discussion

CAP is believed to be a heterogeneous disorder, either in the range of the causative organisms or in the response of the affected host [11]. Although being an acute illness, CAP is associated with long-term morbidity and mortality even after apparent recovery leading to extra costs and consumption of available resources [12].

Platelets are well known to play an important role in both the coagulation system and the host defense against different microbial agents. Hence, platelet count might be considered as an additional marker to judge the severity of illness in patients hospitalized with CAP [13].

In the current study, it was found that the number of CAP patients with thrombocytosis was 33 with a percentage of 13.2%, while, the number of CAP patients with thrombocytopenia was 15 with a percentage of 6% of all hospitalized patients with CAP. This is consistent with the study carried out by Mirsaeidi et al. who showed that 13% of CAP patients presented with thrombocytosis and 5% presented with thrombocytopenia [13].

In this study, it was found that CAP patients with thrombocytosis were younger with a mean age of 54.2 ± 12.6 years compared to CAP patients with normal platelet count with mean age 59 ± 19 and CAP patients with thrombocytopenia with mean age of 73 ± 9.5. This is consistent with the study by Prina et al. who stated that younger patients are healthier with more strong inflammatory response so there is an increase of the platelet count as a part of the inflammatory response while older patients have more frequent comorbidities and less inflammatory response so there is decreased platelet count [5].

In this study, the CURB-65 severity score was significantly higher among CAP patients with thrombocytopenia when compared to those patients with normal platelet count or those with thrombocytosis. This could be explained that thrombocytopenia is associated with more severe pneumonia.

In the current study, respiratory complications including pleural effusion, empyema, and lung abscess were significantly higher among patients with thrombocytosis when compared to patients with thrombocytopenia or patients with normal platelet count. This is adherent to other studies by Chalmers et al. and Prina et al. That could be referred to the tendency of compartmentalization of infection with thrombocytosis [5, 14].

Pleural effusion is common among patients with CAP. It may develop in up to 57% of patients hospitalized with pneumonia. Furthermore, pleural effusion is considered to be a marker of pneumonia severity and is linked to an increased risk of treatment failure [15]. Empyema is recognized to be associated with unfavorable outcomes in CAP and is a common etiology of prolonged treatment (either medical or surgical) and hospital stay [14].

Table 4 Distribution of respiratory complications among all studied groups

Res. comp.	Group			Total (n = 250)	χ^2	p value
	Group I (n = 15)	Group II (n = 202)	Group III (n = 33)			
Lung abscess	0	2 (0.9%)	2 (6.1%)	4 (1.6%)	8.43	0.02[a]
Empyema	0	5 (2.4%)	6 (18.2%)	11 (4.4%)	20.8	< 0.001[a]
Pleural effusion	3 (20%)	30 (14.9%)	12(36.3%)	45 (18%)	8.91	0.01[a]

Group I, thrombocytopenia; group II, normal platelet count; group III, thrombocytosis *Res. comp.* respiratory complications
[a]Difference between group III and other groups

Table 5 Distribution of severe sepsis and septic shock among all studied groups

Parameter	Group			Total (n = 250)	χ^2	p value
	Group I (n = 15)	Group II (n = 202)	Group III (n = 33)			
Severe sepsis	10 (66.7%)	68 (33.7%)	9 (27.3%)	87 (34.8%)	7.65	0.02[a]
Septic shock	8 (53.3%)	40 (19.8%)	5 (15.2%)	53 (21.2%)	7.23	0.03[a]

Group I, thrombocytopenia; group II, normal platelet count; group III, thrombocytosis
[a]Difference between group I and other groups

Table 6 ICU admission and length of hospital stay among all studied groups

Parameter	Group			χ^2	p value
	Group I (n = 15)	Group II (n = 202)	Group III (n = 33)		
ICU admission	8 (53.3%)	17 (8.4%)	4 (12.1%)	27.48	0.000[a]
Length of hospital stay	8.7 ± 4.1	9.5 ± 4.6	10.4 ± 5.9	0.735*	0.480

Group I, thrombocytopenia; group II, normal platelet count; group III, thrombocytosis; *ICU* intensive care unit
*One-way ANOVA is used
[a]Difference between group I and other groups

Table 7 Distribution of need for mechanical ventilation among all studied groups

Parameter	Group			Total (n = 250)	χ^2	p value
	Group I (n = 15)	Group II (n = 202)	Group III (n = 33)			
Non-invasive mechanical ventilation	2 (13.3%)	4 (2%)	1 (3%)	7 (2.8%)	6.31	0.047[a]
Invasive mechanical ventilation	3 (20%)	8 (4%)	1 (3%)	12 (4.8%)	8.12	0.017[a]

Group I, thrombocytopenia; group II, normal platelet count; group III, thrombocytosis
[a]Difference between group I and other groups

Table 8 Readmission and mortality among all studied groups

Parameter	Group			Total (n = 250)	χ^2	p value
	Group I (n = 15)	Group II (n = 202)	Group III (n = 33)			
30 days readmission	6 (40%)	32 (15.8%)	12 (36.4%)	50 (20%)	7.92	0.034[a]
30 days mortality	3 (20%)	10 (5%)	5 (15.2%)	18 (7.2%)	8.33	0.016[a]

Group I, thrombocytopenia; group II, normal platelet count; group III, thrombocytosis
[a]Difference between group II and other groups.

Table 9 Predictors of 30 days mortality among hospitalized patients with CAP in this study

Variable	OR	*P*-value
Septic shock	1.340	0.000
Age > 65 years	2.168	0.002
Confusion at admission	2.443	0.006
Thrombocytopenia	2.692	0.012
PaO_2/FIO_2 < 200 mmHg	3.050	0.017
Thrombocytosis	3.864	0.029

Multivariate logistic regression analysis
CAP community-acquired pneumonia, *OR* odds ratio, PaO_2 partial arterial oxygen pressure, FIO_2 fraction of inspired oxygen

CAP is one of the most common etiologies of severe sepsis and septic shock resulting in up to 45% of cases admitted to hospitals [16]. In this work, it was observed that severe sepsis and septic shock were more common in patients with thrombocytopenia. This is consistent with other studies by Mirsaeidi et al. and Prina et al. That could be attributed to loss of effect of platelets that tend to quarantine the infection resulting in spread of infection with the occurrence of more systemic complications [5, 13].

Thrombocytopenia is frequently encountered in patients admitted to ICU with severe sepsis and septic shock. Patients with thrombocytopenia developed more attacks of life-threatening bleeding, increased occurrence of acute kidney injury, and longer ICU stay. Persistent thrombocytopenia was linked to higher 28-day mortality [17].

Different mechanisms are implicated in the occurrence of thrombocytopenia in patients with sepsis. In sepsis, platelets are believed to be activated and adhere to the endothelium, leading to their sequestration and destruction. Immune-mediated mechanisms like nonspecific platelet-associated antibodies and cytokine-driven hemophagocytosis of platelets can also contribute to sepsis-induced thrombocytopenia [18].

In the current study, CAP patients with thrombocytopenia significantly needed mechanical ventilation either invasive or even non-invasive, when compared to CAP patients both with thrombocytosis or with normal platelet count.

CAP patients with acute respiratory failure (ARF) often need non-invasive ventilatory support. Invasive mechanical ventilation is indicated in patients with life-threatening ARF or in those who have failed to respond to non-invasive ventilation (NIV) treatment [19].

Results of this study showed that CAP patients with thrombocytopenia and CAP patients with thrombocytosis had significant 30 days readmission and significant 30 days mortality when compared to CAP patients with normal platelet count. This could be attributed to more frequent complications and more severe pneumonia among those patient [12, 13].

In the current study, 30 days mortality was independently associated with septic shock, older age more than 65 years, confusion at admission, thrombocytopenia, PaO2/FIO2 < 200 mmHg, and thrombocytosis.

This is consistent with other studies by Laserna et al. and Prina et al. [5, 20].

While thrombocytosis and thrombocytopenia as shown in this study and other studies are important factors in predicting morbidity & mortality in CAP, complications with thrombocytosis were more as local complications in the form of lung abscess, empyema, and pleural effusion while complications with thrombocytopenia were more as general complications in the form of severe sepsis and septic shock. Higher mortality in CAP patients with thrombocytosis could be attributed to insufficient management of the respiratory complications for several causes, e.g., late diagnosis and drainage, inadequate antibiotic, inadequate treatment duration, or absence of adequate follow-up [5]. The prognostic impact of platelets in patients admitted to ICU for severe CAP was demonstrated since the lower was the initial platelet count, the higher was the mortality rate [21].

This study had the following limitations: first, small number of studied patients; second, causative organisms were not studied to explore their potential relation to platelet count although it showed no significant statistical difference in other studies; third, biomarkers were not analyzed; and finally, we recommend inclusion of thrombocytosis and thrombocytopenia in severity assessment of patients with CAP. Also, further studies on platelet count in CAP patients to evaluate its impact on the outcome are needed.

Conclusions

Thrombocytopenia in patients with CAP is associated with more severe pneumonia, severe sepsis, septic shock, need for ICU admission, need for invasive M.V, and poor outcome. While, thrombocytosis in patients with CAP is associated with more respiratory complications as regard lung abscess, empyema and pleural effusion, and poor outcome.

Abbreviations

CAP: Community-acquired pneumonia; ABG_S: Arterial blood gases; ICU: Intensive care unit; PaO_2: Partial arterial oxygen pressure; FIO_2: Fraction of inspired oxygen; BUN: Blood urea nitrogen; WBC_S: White blood cells; IDSA: Infectious Disease Society of America; ATS: American Thoracic Society; ARF: Acute respiratory failure; NIV: Non-invasive ventilation; MV: Mechanical ventilation

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Authors' contributions

AG and MM were responsible for the study concept and design. SE and ME were responsible for patient selection, acquisition, analysis, and interpretation of data. Preparation of the draft was carried out by SE. The manuscript was

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Availability of data and materials
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Ethics approval and consent to participate
This study was approved by the Ethics Committee of Zagazig, Faculty of Medicine. The committee's reference number is not applicable. An informed written consent was collected from all participants.

Consent for publication
Consent was obtained from all contributors.

Competing interests
The authors declare that they have no competing interests.

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