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Mean platelet volume and D-dimer as predictors for complicated community-acquired pneumonia in hospitalized children

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Abstract

Background Community-acquired pneumonia (CAP) is one of the primary causes of child mortality and morbidity. The primary objective of our research was to assess the value of mean platelet volume (MPV) and D-dimer levels in predicting complicated community-acquired pneumonia in hospitalized children.

Methods This observational retrospective study gathered medical data from the electronic medical records of children diagnosed with CAP who were admitted to the Pediatric Pulmonology Unit between December 2021 and December 2022.

Results This study included 154 pediatric patients. Their age at presentation was 4.15 ± 3.60 years. A comparison of patients with complicated CAP and non-complicated CAP revealed a statistically significant decrease of MPV in the complicated CAP group than in the non-complicated group ($p = 0.016$). The D-dimer level was significantly higher in the complicated CAP 3.42 ± 3.02 µg/ml compared than in the non-complicated 1.63 ± 2.04 µg/ml, $p = 0.002$). Low MPV and increased D-dimer were powerful indicators of complicated CAP (OR 0.577, $p = 0.021$, OR 1.419, $p = 0.003$).

Conclusion The current study highlights that low MPV and high D-dimer levels can be useful predictors of pulmonary complications of CAP in children. However, prospective observational studies are needed to evaluate the changes in these predictors during the disease and assess the time needed for normalization.

Keywords Children, Complications, D-dimer, Mean platelet volume, Pneumonia

Background

Community-acquired pneumonia is the term used to describe lower respiratory tract infections in children that occurred outside of a hospital setting [1]. By identifying those who are prone to develop complications, clinicians may be able to determine which CAP patients may need closer supervision and when to start more intensive therapy [2].

A high index of suspicion is needed to anticipate pulmonary complications, especially if a child becomes unwell or develops a fever 48 h after initiating medication. These complications can include lung abscesses, necrotizing pneumonia, pleural effusion, and/or empyema [3].

Empyema and parapneumonic effusion are thought to be separate stages of the same pathophysiological process, while necrotizing pneumonia is a rare but serious complication in children. It can be identified by a

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prolonged clinical course in children who were previously healthy despite getting an appropriate antibiotic regimen [4, 5].

Reactive thrombocytosis, one of the many acute-phase reactants that are triggered in inflammatory conditions such as pneumonia, results in increased platelet count and decreased mean platelet volume (MPV). Due to this mechanism, numerous studies looked at how MPV affected various inflammatory and infectious disorders [6].

D-dimer was initially used to identify acute thrombotic conditions, such as pulmonary embolism. Recently, it has been used as a warning sign of serious inflammation and infection. As D-dimer levels are closely related to the inflammatory response, they may provide insight into how an infection influences the coagulation system in infectious conditions. According to several studies, there is a strong correlation between the severity of community-acquired pneumonia and D-dimer level [7].

Our goal was to determine the value of MPV and D-dimer levels in predicting complicated community-acquired pneumonia in hospitalized children.

Methods

Data collection

The medical records of patients admitted to the Pediatric Pulmonology Unit were searched to find patients who were diagnosed with CAP between December 2021 and December 2022. This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the research ethics committee of the Faculty of Medicine under the number 36246/12/22. The need for informed consent was waived by the ethics committee of the Faculty of Medicine because of the retrospective nature of the study.

All children aged between 2 months and 18 years who fulfilled the diagnostic criteria of CAP were included in the study. CAP was defined as the presence of signs and symptoms of pneumonia in a previously healthy child who acquired infection outside the hospital and radiological findings of lung consolidation [8].

Children who have an underlying immunodeficiency, chronic lung illness, cancer, congenital lung malformations, and/or neuromuscular diseases that affected respiration and patients with missing data were excluded from the search. The patients were divided into groups based on the occurrence of complications.

Demographic data, such as sex, age, and characteristics of the initial clinical manifestations, age at diagnosis, antibiotic therapy, length of hospital stay, occurrence of complications, need for surgical intervention or chest tube insertion, as well as laboratory tests CBC, D-dimer, CRP, procalcitonin, and pleural fluid analysis and culture were included.

Statistical analysis

Data were collected and entered into a spreadsheet using Microsoft Excel 2020. Statistical analyses were performed using the SPSS version 23. Quantitative data with a normal distribution are presented as means and standard deviations (m ± SD), whereas categorical data are presented as numbers and percentages. Student's *t*-test was used to compare quantitative variables, while χ^2 tests were used to compare qualitative variables. Logistic regression was used to identify the predictive power of MPV and D-dimer levels for complicated CAP. The Hosmer–Lemeshow test was employed to assess the goodness-of-fit of the logistic regression models. Receiver operating characteristic (ROC) curves were used to assess the sensitivity and specificity of MPV and D-dimer levels for predicting complicated CAP. The level of significance was set at $p < 0.05$.

Results

Patient characteristics

According to the medical records review, 210 patients diagnosed with CAP between December 2021 and December 2022 were identified. Of these, 154 patients met the inclusion criteria. The average age of our cohort was 4.15 ± 3.6 years, with fifty-seven (57%) being males. Left lower lobar pneumonia was the most common primary diagnosis, affecting 68 patients (31.8%), followed by right lower lobar pneumonia and whole right pneumonia, affecting 50 (23.4%) and 44 (20.6%) patients, respectively. Sixty patients (38.9%) experienced complications, with necrotizing pneumonia (33.6%) being the most common complication (Table 1).

Patients with complicated CAP had a significantly longer length of hospital stay and fever duration ($p < 0.001$) (Table 2).

Our patients did not experience any vascular or hematological problems or received any treatment for this.

Laboratory parameters

Complicated CAP showed a statistically significant increase in lymphocyte count and a decrease in MPV compared to the non-complicated group ($p = 0.006$ and $p = 0.016$, respectively).

The D-dimer level was significantly higher in the complicated CAP 3.42 ± 3.02 µg/ml compared than in the non-complicated 1.63 ± 2.04 µg/ml, $p = 0.002$). Compared to patients with other complications, patients with necrotizing pneumonia had the highest D-dimer level 3.37 ± 3.22 (Table 2).

Table 1 Demographic and clinical features of patients

Variables	Total† (*n* = 154)	Non complicated† CAP (*n* = 94)	Complicated† CAP (*n* = 60)	*P* value
Gender				
■ Male	122 (57.0%)	54 (57.4%)	34 (56.7%)	0.936
■ Female	92 (43.0%)	40 (42.6%)	26 (43.3%)	
Clinical manifestations				
■ Fever	154 (100.0%)	94 (100.0%)	60 (100.0%)	
■ Dyspnea	154 (100.0%)	94 (100.0%)	60 (100.0%)	
■ Cough	108 (50.5%)	56 (59.6%)	26 (43.3%)	0.095
■ Grunting	84 (39.3%)	20 (21.3%)	32 (53.3%)	0.001*
■ Chest pain	14 (6.5%)	4 (4.3%)	5 (8.3%)	0.397
■ GIT manifestations	18 (8.4%)	6 (6.4%)	6 (10.0%)	0.503
■ Hemoptysis	2 (0.9%)	2 (2.1%)	0 (0.0%)	0.256
■ Pallor	6 (2.8%)	6 (6.4%)	0 (0.0%)	0.047*
Diagnosis				
■ Pneumonia	94 (43.9%)	94 (43.9%)	0 (0.0%)	
■ PPE	42 (19.6%)	0 (0.0%)	21 (35.0%)	< 0.001*
■ Lung abscess	6 (2.8%)	0 (0.0%)	3 (5.0%)	
■ NP	72 (33.6%)	0 (0.0%)	36 (60.0%)	
Ineffective EAT	126 (58.9%)	28 (22.2%)	49 (77.8%)	< 0.001*

† Presented as number (percentage), *statistical significant set at $p \leq 0.05$, χ^2 chi-square test

CAP community-acquired pneumonia, *PPE* parapneumonic effusion, *NEC* necrotizing pneumonia, *Rt* right, *Lt* left, *EAT* empirical antimicrobial therapy

Table 2 Laboratory parameters in complicated and non-complicated CAP patients

Variables†	Total (*n* = 154)	Non-complicated CAP (*n* = 94)	Complicated CAP (*n* = 60)	*P* value
Age (year)	4.15 ± 3.60	4.45 ± 3.33	3.91 ± 2.83	0.301
Length of hospital stay (days)	12.37 ± 6.89	8.28 ± 4.71	15.58 ± 6.65	< 0.001*
Duration of symptoms before hospitalization (days)	4.86 ± 3.28	2.66 ± 2.04	6.58 ± 3.03	< 0.001*
Duration of fever (days)	3.95 ± 2.88	2.66 ± 1.80	4.98 ± 3.16	< 0.001*
Duration of cavitation (days)	6.44 ± 4.89		6.44 ± 4.89	
RR (breath/minute)	52.51 ± 9.08	50.45 ± 9.17	54.13 ± 8.75	0.015*
Hb (g/dl)	9.64 ± 1.56	9.64 ± 1.83	9.64 ± 1.33	0.985
Hct %	29.99 ± 4.95	29.81 ± 5.26	30.13 ± 4.72	0.702
WBCs (103/μL)	18.50 ± 9.32	17.70 ± 8.36	19.13 ± 10.03	0.340
Neutrophils (109/L)	13.69 ± 7.56	13.87 ± 7.39	13.54 ± 7.76	0.791
Lymphocytes (109/L)	3.73 ± 2.82	2.89 ± 1.74	4.39 ± 3.31	< 0.001*
Monocytes (109/L)	0.94 ± 0.74	0.81 ± 0.54	1.05 ± 0.85	0.034*
Platelets (109/L)	422.45 ± 215.79	386.43 ± 168.55	450.07 ± 243.75	0.077
MPV (fl)	8.93 ± 1.16	9.26 ± 1.08	8.59 ± 1.15	< 0.001*
PCT %	0.39 ± 0.19	0.344 ± 0.132	0.428 ± 0.221	0.004*
PDW (fl)	11.26 ± 2.02	11.31 ± 2.04	11.21 ± 2.03	0.767
CRP (mg/l)	110.72 ± 81.41	110.14 ± 74.85	111.45 ± 90.20	0.922
D-dimer (μg/ml)	2.63 ± 2.76	1.63 ± 2.04	3.42 ± 3.02	< 0.001*

† Presented as mean ± standard deviation, **P* statistical significance set at $p \leq 0.05$, *t* independent *t*-test

RR respiratory rate, *HB* hemoglobin, *Hct* hematocrit, *WBCs* white blood cells, *MPV* mean platelet volume, *PCT* platelet crit, *PDW* platelet distribution width, *CRP* C-reactive protein

Thirty-four patients underwent pleural fluid analysis. Twenty-nine (85.3%) patients had empyema and five (14.7%) had parapneumonic effusion. The median (IQR) total leucocytic count was 15,600.0 (3175.0–59,825.0) cells/mm^3, whereas the median (IQR) LDH was 6812.0 (1178.0–13,700.0) units/L. Please refer to (Fig. 1) for the remaining pleural fluid analysis results.

Pleural fluid culture results were positive for 17 patients. *Staphylococcus aureus*, Streptococcus *pneumoniae*, and MRSA were the most prevalent organisms in 6, 3, and 2 cases, respectively.

Binary logistic regression analysis of MPV and D-dimer as Predictors of complicated CAP

To identify the prognostic power of MPV and D-dimer for the prediction of complicated CAP, univariate logistic regression analysis was conducted (Table 3).

The area under the ROC curve for D-dimer to predict complicated CAP was 0.759 (95% CI 0.665–0.852, $p < 0.001$) with a sensitivity of 81.8% and a specificity of 57.4% at the best cutoff point of 1.17 µg/ml (Fig. 2), while the area under the curve for MPV was very low, indicating its poor predictive power for complicated CAP.

Table 3 Logistic regression analysis for the predictors of complicated CAP

Variable	Univariate analysis	
	OR (CI 95%)	*P* value*
MPV (fl)	0.577 (0.362–0.919)	0.021
D-dimer (µg/ml)	1.419 (1.127–1.787)	0.003

* Statistical significance set at $p \leq 0.05$, *OR* odds ratio, *MPV* mean platelet volume

Discussion

A cohort of 154 patients with CAP was included in this study. The findings indicated that 38.9% of patients had complicated CAP and 61.0% had non-complicated CAP. Similar to earlier studies [9, 10]. our analysis revealed a high prevalence of complicated CAP, which was clearly observed in the post COVID-19 pandemic era.

We observed that patients with complicated CAP had a significantly longer hospital stay (15.58 ± 6.65 vs 8.28 ± 4.71 days) and longer duration of fever (4.98 ± 3.16 vs 2.66 ± 1.80 days) which is in line with the findings of Wexler et al. [11]. who reported that complicated CAP patients had a longer hospital stay (13.2 ± 11.3 vs 8.3 ± 8.3 days) and a longer duration of fever (9.2 ± 7.0 vs 5.1 ± 5.7 days). Similar findings were also shown by Chalmers et al. [12].

The MPV is a commonly used parameter measured in the CBC. Increased MPV can be used as a metric for platelet activation and production rate. The consumption and sequestration of large platelets in the vascular segments of the inflammatory zone may result in a reduction in MPV during high-grade inflammation. While Karadag-Oncel et al. [13]. utilized healthy controls for comparison and employed non-complicated CAP, the MPV in the current study was significantly lower in complicated CAP, which is consistent with their findings.

In contrast, complicated CAP was linked to higher MPV than uncomplicated CAP, according to Hashemian et al. [14]. and Bekdas et al. [15]. The first study only included CAP complicated by empyema. However, the second study had a small sample size (9 patients), which may have skewed the findings. Prior research has suggested links between high MPV and pneumonia severity; however, more research is needed to confirm the link between MPV and the emergence of complicated CAP.

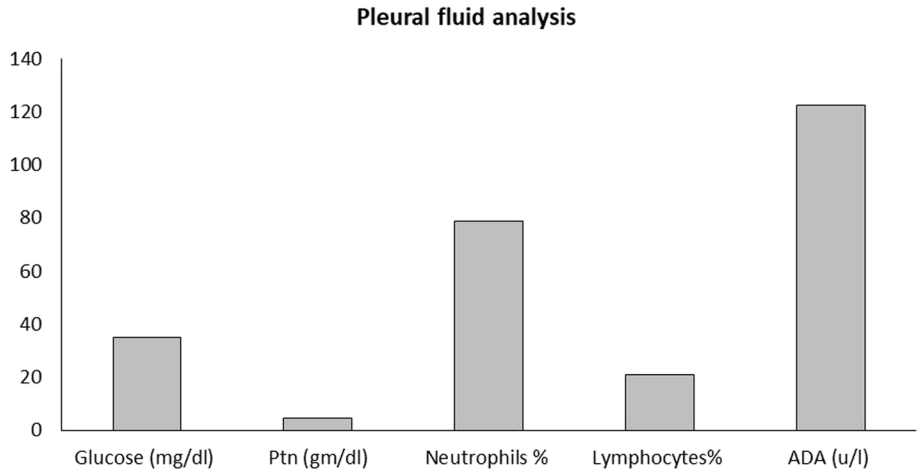

Fig. 1 Bar chart showing the pleural fluid analysis results

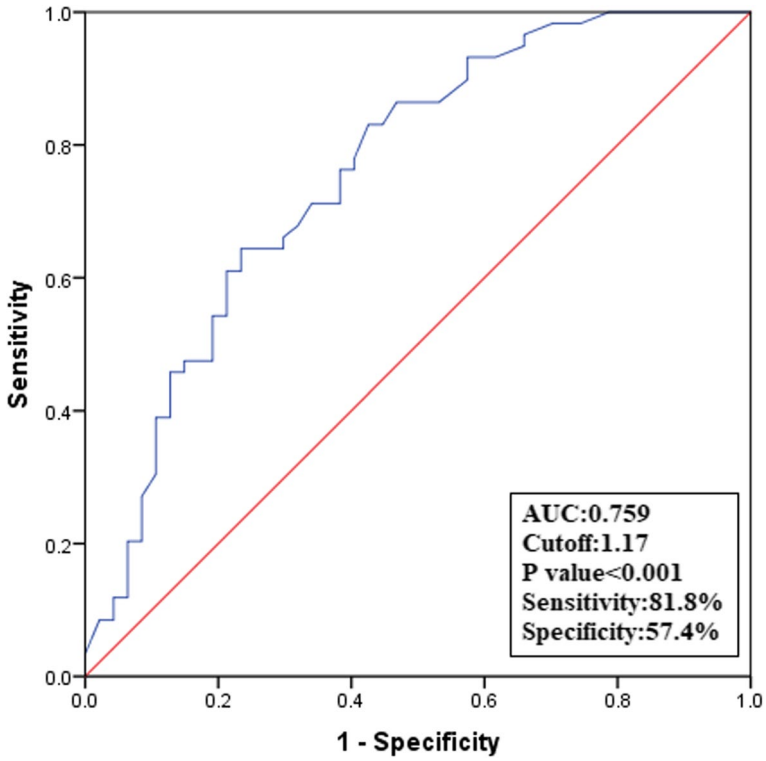

Fig. 2 ROC curve of D-dimer for predicting complicated community-acquired pneumonia

D-dimer level is an objective biomarker that reflects coagulation and fibrinolysis. Inflammation–coagulation imbalance plays an important role in the formation of parapneumonic effusion and lung necrotization. The results of prior research coincide with the findings of this study, which found that complicated CAP patients had significantly raised D-dimer levels, indicating a disturbance of coagulation and fibrinolysis in the development of complicated pneumonia [16, 17].

Elevated D-dimer levels may indicate that hypercoagulability is more common and severe in children with complicated CAP than in those without complications.

We anticipated considerably higher CRP levels in children with complicated CAP; therefore, our results were surprising. The fact that there was no discernible difference between the two groups may have been caused by the long-term nature of the condition and the usage of antibiotics before admission. Therefore, identifying additional inflammatory biomarkers to determine the presence of complicated CAP is mandatory.

We believe that our study is the first to employ MPV and D-dimer as predictors of complicated CAP in children.

Study limitations

As this study was retrospective, some patient data were not accessible for comparison or analysis. We were unable to stratify complicated CAP to determine the potential predictive factors for each complication type due to the relatively limited sample size. In addition, the data may be affected by previous treatment, duration of illness, and causative organisms.

Conclusion

We concluded that measuring D-dimer level and MPV in children with CAP on admission could provide extra benefits in predicting the pulmonary complications of CAP.

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Authors' contributions

RE made substantial contribution to the concept and design of the work. OE contributed to the data interpretation and data acquisition. AM drafted the work and revised it. All authors read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available upon reasonable request from the corresponding author.

Declarations

Ethics approval and consent to participate
This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the research ethics committee of the Faculty of Medicine, Tanta University, under the number 36246/12/22. The need for informed consent was waived by the ethics committee of the Faculty of Medicine, Tanta University, because of the retrospective nature of the study.

Consent for publication
Not applicable.

Competing interests
The authors have no potential conflicts of interest regarding the research, authorship, and/or publication of this article.

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References

1. Bradley JS, Byington CL, Shah SS et al (2011) Pediatric Infectious Diseases Society and the Infectious Diseases Society of America. The management of community-acquired pneumonia in infants and children older than 3 months of age: clinical practice guidelines by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America. Clin Infect Dis 53(7):e25-76
2. Masarweh K, Gur M, Toukan Y et al (2021) Factors associated with complicated pneumonia in children. Pediatr Pulmonol 56(8):2700–2706
3. Esposito S, Dal Canto G, Caramia MR et al (2022) Complications in community acquired pneumonia: magnitude of problem, risk factors, and management in pediatric age. Expert Rev Anti Infect Ther 20(1):45–51
4. Masters IB, Isles AF, Grimwood K (2017) Necrotizing pneumonia: an emerging problem in children? Pneumonia (Nathan) 9:11
5. de Benedictis FM, Kerem E, Chang AB, Colin AA, Zar HJ, Bush A (2020) Complicated pneumonia in children. Lancet 396(10253):786–798
6. Zareifar S, Farahmand Far MR, Golfeshan F, Cohan N (2014) Changes in platelet count and mean platelet volume during infectious and inflammatory disease and their correlation with ESR and CRP. J Clin Lab Anal 28(3):245–248
7. Ge YL, Liu CH, Wang N, et al (2019) Elevated plasma D-dimer in adult community-acquired pneumonia patients is associated with an increased inflammatory reaction and lower survival. Clin Lab 65(1):131.
8. Tuğcu GD, Özsezen B, Türkyılmaz İ et al (2022) Risk factors for complicated community-acquired pneumonia in children. Pediatr Int 64(1):e15386
9. Harris M, Clark J, Coote N et al (2011) British thoracic society standards of care committee. British thoracic society guidelines for the management of community acquired pneumonia in children: update 2011. Thorax 66(Suppl 2):ii1–ii23
10. Oktafia P, Airlangga PS, Dharmawati I, Setyoningrum RA (2021) Risk factors of complicated pneumonia in children. J Indon Med Assoc 71(3):135–140
11. Wexler ID, Knoll S, Picard E et al (2006) Clinical characteristics and outcome of complicated pneumococcal pneumonia in a pediatric population. Pediatr Pulmonol 41(8):726–734
12. Chalmers JD, Singanayagam A, Murray MP, Scally C, Fawzi A, Hill AT (2009) Risk factors for complicated parapneumonic effusion and empyema on presentation to hospital with community-acquired pneumonia. Thorax 64(7):592–597
13. Karadag-Oncel E, Ozsurekci Y, Kara A et al (2013) The value of mean platelet volume in the determination of community acquired pneumonia in children. Ital J Pediatr 39:16
14. Hashemian H, Sanati F (2022) Comparing the mean platelet volume and the neutrophil-to-lymphocyte ratio in children with bacterial pneumonia associated with or without pleural empyema. J Guilan Univ Med Sci 31(4):328–337
15. Bekdas M, Göksügür SB, Sarac EG et al (2014) Neutrophil/lymphocyte and C-reactive protein/mean platelet volume ratios in differentiating between viral and bacterial pneumonias and diagnosing early complications in children. Saudi Med J 35(5):442–447
16. Shen Y, Yang T, Jia L et al (2013) A potential role for D-dimer in the diagnosis of tuberculous pleural effusion. Eur Rev Med Pharmacol Sci 17(2):201–205
17. Marinkovic SP, Topuzovska IK, Milenkovic Z et al (2016) The role of serum coagulation factors in the differential diagnosis of patients with pneumonia and parapneumonic effusion. Pril (Makedon Akad Nauk Umet Odd Med Nauki) 37(2–3):81–88

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