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# The role of immature granulocytes in the early diagnosis of pneumonia developing secondary to rib fractures

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## ABSTRACT

**Aims:** This retrospective study aimed to investigate the role of immature granulocytes (IGs) in the early diagnosis of pneumonia secondary to rib fractures.

**Methods:** This study was conducted on patients who applied to the emergency department of our hospital between 2019 and 2022. Patients aged between 18 and 100 years who were found to have rib fractures in the thorax CT report and were hospitalized, who had hemogram data in the hospital's database, were included in the study. Patients with detected COVID-19 infection without hemogram data and patients who refused examination and treatment were excluded from the study. Patients' blood tests, radiological images, and epicrisis reports were analyzed. The data of patients with and without pneumonia were compared statistically.

**Results:** Overall, 155 patients, 117 men and 38 women were included in the study. Pneumonia developed in 11 patients, and two patient died. In our study, it was determined that the risk of pneumonia increased by 38% in each additional rib fracture, and the risk of pneumonia increased 9.44 times if the IG value at the 48$^{th}$ hour was greater than 0.06. In addition, when the receiver operating characteristic curves in our study were examined, it was observed that the IG number at 48 hours gave excellent results in the diagnosis of pneumonia, with 75% sensitivity and 88% specificity (cut off: 0.055, AUC: 0.827, p=0.002).

**Conclusion:** Our study showed that IGs are an effective marker in the early diagnosis of pneumonia secondary to rib fractures.

**Keywords:** Rib fracture, pneumonia, immature granulocytes, CRP

## INTRODUCTION

One of the most common pathologies observed in blunt thoracic trauma is rib fracture. Rib fractures are observed in 10% of patients with blunt thoracic traumas.[1] Rib fractures can cause conditions that require emergency intervention, such as hemothorax, pneumothorax, and lung contusion. In addition, hypoventilation and atelectasis may develop due to pain. If atelectasis continues for a long time, pneumonia and acute respiratory distress syndrome (ARDS) may develop. The incidence of pneumonia due to rib fractures varies between 6% and 27% in studies.[2,3] Therefore, early diagnosis of pneumonia developing in trauma patients and initiation of appropriate antibiotic therapy are vital.

Pneumonia developing secondary to rib fractures occurs mostly in the hospital-acquired pneumonia group because there is no pneumonia at the time of admission to the hospital, and it mostly develops during the hospitalization period. It has different clinical features from community-acquired pneumonia. One of the main differences is an inflammatory response resulting from the trauma itself. This inflammatory response complicates the diagnosis of pneumonia. The second difference is exposure to the common disruptive effects of both thoracic trauma and pneumonia in the respiratory system. The third difference is that the clinical picture is more complicated due to extrathoracic trauma (cranial injury, abdominal injury, orthopedic injuries). The fourth difference is that pneumonia due to rib fractures is predictable. This predictability opens a window of opportunity for early diagnosis and treatment.

Fever, sputum, dyspnea, rales on auscultation, leukocytosis, increased C-reactive protein (CRP), reproduction in sputum culture, and radiological pneumonic infiltrates play a role in diagnosing pneumonia. However, it is not always easy to diagnose pneumonia after thoracic trauma. There are various reasons for this. Pulmonary contusion, which is very common in thoracic trauma, can mimic pneumonia radiologically. Another reason is atelectasis due to pain and shallow breathing in patients with thoracic trauma. Although atelectasis is not considered infected at first, pneumonia may develop in the lung that remains atelectatic for a long time.[4] Furthermore, there

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are laboratory tests and radiological images that complicate the diagnosis of pneumonia. Since CRP is a nonspecific test, it can increase both in trauma and pneumonia, making the diagnosis difficult. Similarly, leukocytosis, which develops as an inflammatory response secondary to trauma, may cause false positives in the diagnosis of pneumonia. A delay in diagnosis can lead to increased morbidity and mortality. Moreover, false positivity in the diagnosis can lead to undesirable results, such as unnecessary antibiotic use, antibiotic resistance, and drug side effects.

There are also inflammation markers not yet included in the clinical routine in diagnosing pneumonia. For example, immature granulocytes (IGs) in peripheral blood reflect the bone marrow response to bacterial infection. IG is classified by microscopic examination as promyelocytes, myelocytes, and metamyelocytes.[5,6] Advances in technology have enabled automated hematology analyzers to count IGs.[7]

This study aims to investigate the role of IGs in the early diagnosis of pneumonia secondary to rib fracture.

## METHODS

This study was conducted on patients who applied to the emergency department of our hospital between 2019 and 2022. The patients' clinical, radiological, and laboratory data were collected retrospectively from the hospital's database. Before starting the study, approval was obtained from Kastamonu University Clinical Researches Ethics Committee (Date: Decision No: 2022-KAEK-58). In the study, the principles of the Declaration of Helsinki were adhered to.

Patients aged between 18 and 100 years, who were found to have rib fractures in the thorax CT report and were hospitalized, who had hemogram data in the hospital's database, were included in the study. Patients who were diagnosed with COVID-19 infection, did not have hemogram data, were referred out of the province, and refused examination and treatment were excluded from the study.

The following criteria were used as an indication for hospitalization in patients with rib fractures: Patients with three or more rib fractures, concomitant hemothorax or pneumothorax condition, patients over 65 years old with rib fractures, first rib fractures, and patients hospitalized for serious concomitant extrathoracic trauma.

During their hospitalization, daily hemograms and chest X-rays were routinely done on the patients, and their vital signs were monitored. In addition, paracetamol and dexketoprofen were administered to the patients as routine analgesic treatments. Opioid analgesics were administered as needed. Routine prophylactic antibiotics were not administered.

Infectious diseases consultation was done with patients with fever, sputum, dyspnea, rales on auscultation, leukocytosis, increased CRP, reproduction in sputum culture, and radiological pneumonic infiltration. All pneumonia diagnoses were made by an infectious diseases specialist. Antibiotherapy was started with the recommendation of the infectious diseases specialist for the patients diagnosed with pneumonia.

Blood tests were taken during the initial admission and 24 and 48 hours after the patients were analyzed. Hemogram parameters were calculated with an automated hematological analyzer (XN-1000 Hematology Analyzer Sysmex Corporation, Japan).

The data of patients with and without pneumonia diagnosis were compared using the Statistical Package for Social Sciences 23.0 for Windows (SPSS Inc., Chicago, USA) program. Descriptive statistics are given as numbers and % for categorical variables. Continuous data are given as median (25% percentiles, 75% percentiles). Chi-square and Fischer's exact tests were used to analyze categorical data. Mann Whitney U test was used to compare the mean values. Receiver operating characteristic (ROC) analysis was performed, and Youden's index was used to determine the area under the curve (AUC), cut-off, specificity, and sensitivity. Finally, binary logistic regression analysis was used in univariate and multivariate analyses.

## RESULTS

One hundred and sixty-seven patients were evaluated for eligibility for the study. Twelve patients were excluded from the study-eight were due to COVID-19 infection, three patients' hemogram data could not be accessed, and one patient refused examination and treatment. Overall, 155 patients, 117 men and 38 women, who met the inclusion criteria were included in the study (Figure 1).

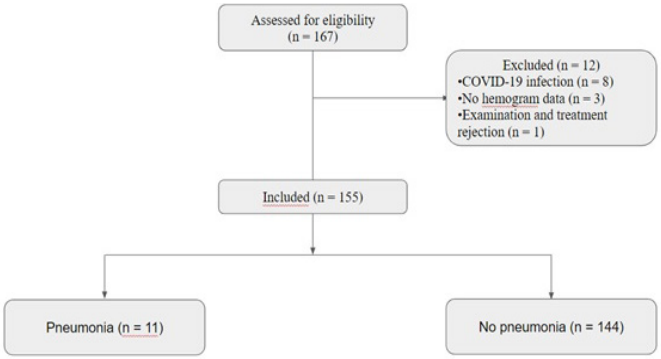


**Figure 1.** Consort diagram

Pneumonia developed in 11 of the patients included in the study, while no sign of pneumonia was observed in 144 patients. The median age was 66 (59; 86) in the pneumonia group. The median age was 65 (55; 72.75) in the group without pneumonia. There was no significant age difference between the groups (p=0.314). In the group that developed pneumonia, 10 patients (91%) were male, and one was female (9%; p=0.296). The most common etiologies for rib fractures were falls and motor vehicle accidents. No significant correlation was observed between the etiologic causes and the development of pneumonia (p=0.635). Six patients (54%) who developed pneumonia required intensive care admission. In the group without pneumonia, 11 patients (8%) needed intensive care (p=0.000). The median Charlson score was 3 (2; 5) in the pneumonia group and 2 (1; 3) in the non-pneumonia group (p=0.096). The median number of broken ribs was 4 (4; 7) in the pneumonia group and 3 (2; 5) in the group without pneumonia (p=0.057), while the median Injury Severity Index score was 16 (9; 25) in the pneumonia group and 9 (9; 16) in the non-pneumonia group (p=0.025). The median hospital stay was 7 (6; 14) days in the group with pneumonia and 3 (2; 4) days in the group without pneumonia (p=0.000; Table 1).

In the ROC analysis (Figure 2, Table 2), acceptable and excellent values were obtained for the following parameters: 24$^{th}$-hour WBC (cut off: 11.07, AUC: 0.779), 24$^{th}$-hour IG count (cut off: 0.045, AUC: 0.758), 48$^{th}$-hour WBC (cut off: 12.01, AUC: 0.827), and 48$^{th}$-hour IG count (cut off: 0.055, AUC: 0.827).

**Table 1. Demographic and clinical data of patients**

| | Pneumonia (n=11) | No pneumonia (n=144) | p value |
|---|---|---|---|
| Age, years median (IQR) | 66 (59; 86) | 65 (55; 72.75) | 0.314 |
| Male, n (%) | 10 (91%) | 107 (74%) | 0.296 |
| Etiology | | | |
| Fall, n (%) | 7 (63%) | 91 (63%) | 0.635 |
| MVA, n (%) | 4 (37%) | 43 (29%) | |
| Others, n (%) | 0 (0%) | 10 (8%) | |
| ICU admission, n (%) | 6 (54%) | 11 (7%) | 0.000 |
| Charlson score, median (IQR) | 3 (2; 5) | 2 (1; 3) | 0.096 |
| Fractured ribs, median (IQR) | 4 (4; 7) | 3 (2; 5) | 0.057 |
| ISI score, median (IQR) | 16 (9; 25) | 9 (9; 16) | 0.025 |
| Admission time, days median (IQR) | 7 (6; 14) | 3 (2; 4) | 0.000 |

IQR: Inter quartile range, MVA: Motor vehicle accident, ICU: intensive care unit; ISI: Injury severity index

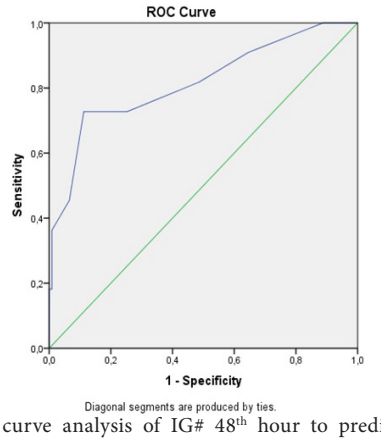


**Figure 2.** ROC curve analysis of IG# 48th hour to predict pneumonia development

ROC: Receiver operating characteristic, IG: Immature granulocyte

**Table 2. ROC curve analysis to predict pneumonia development**

| | Cut-off | AUC | 95% CI | p | Sensitivity | Specificity |
|---|---|---|---|---|---|---|
| CRP* (mg/L) | 20.50 | 0.671 | 0.43-0.90 | 0.109 | 50 | 89 |
| WBC* (×10⁹/L) | 11.79 | 0.625 | 0.42-0.82 | 0.242 | 75 | 55 |
| IG#* (×10⁹/L) | 0.075 | 0.548 | 0.31-0.77 | 0.656 | 75 | 55 |
| IG%* | 2.80 | 0.464 | 0.23-0.69 | 0.733 | 12 | 100 |
| WBC** (×10⁹/L) | 11.07 | 0.779 | 0.58-0.97 | 0.009 | 87 | 69 |
| IG#** (×10⁹/L) | 0.045 | 0.758 | 0.57-0.93 | 0.016 | 75 | 66 |
| IG%** | 0.35 | 0.665 | 0.48-0.84 | 0.123 | 75 | 49 |
| WBC*** (×10⁹/L) | 12.01 | 0.827 | 0.63-1.00 | 0.002 | 75 | 90 |
| IG#*** (×10⁹/L) | 0.055 | 0.827 | 0.64-1.00 | 0.002 | 75 | 88 |
| IG%*** | 0.55 | 0.654 | 0.46-0.84 | 0.150 | 37 | 89 |

*Initial admission, **24th hour, ***48th hour, ROC: Receiver operating characteristic, CRP: C-reactive protein, AUC: Area under the curve, CI: Confidence interval, IG: Immature granulocyte

In univariate logistic regression analysis, Charlson score (OR 1.487, 95% CI 1.018-2.173, p=0.040), the number of broken ribs (OR 1.345, 95% CI 1.054-1.717, p=0.017), CRP (OR 1.016, 95% CI 1.001-1.031, p=0.035), and the 48th-hour IG# (OR 11.905, 95% CI 2.899-48.893, p=0.001) were found to be significantly associated with pneumonia. When multivariate logistic regression analysis was performed, the number of broken ribs (OR 1.385, 95% CI 1.035-1.852, p=0.028) and IG# at 48 hours (OR 9.441, 95% CI 1.865-47.797, p=0.007) were found to be associated with pneumonia (Table 3).

**Table 3. Logistic regression analysis of independent markers of pneumonia**

| | Univariate analysis | | Multivariate analysis | |
|---|---|---|---|---|
| Variables | OR (95% CI) | p | OR (95% CI) | p |
| Charlson score | 1.487 (1.018-2.173) | 0.040 | 1.434 (0.929-2.213) | 0.104 |
| Fractured ribs | 1.345 (1.054-1.717) | 0.017 | 1.385 (1.035-1.852) | 0.028 |
| CRP (mg/L) | 1.016 (1.001-1.031) | 0.035 | 1.009 (0.990-1.028) | 0.373 |
| IG#*** (×10⁹/L)>0.06 | 11.905 (2.899-48.893) | 0.001 | 9.441 (1.865-47.797) | 0.007 |

***48th hour, CI: Confidence interval, OR: Odds ratio, CRP: C-reactive protein, IG: Immature granulocyte

Tube thoracostomy was performed on 20 patients in the study population. Thoracic surgery was not applied to the patients included in the study, except for tube thoracostomy. Two patients died in the study population. A 93-year-old male patient died on the 30th day of hospitalization, and a 71-year-old male patient died on the 6th day of hospitalization. Pneumonia developed in both patients and they were being followed up in the intensive care unit.

## DISCUSSION

In our study, it was determined that the risk of pneumonia increased by 38% in each additional rib fracture, and the risk of pneumonia increased 9.44 times if the IG number at the 48th hour was greater than 0.06.

In the literature, the rate of pneumonia in patients hospitalized for rib fractures varies. While some studies have reported rates as low as 6%,[2] others have reported pneumonia rates as high as 27%.[3] In our study, the rate of pneumonia in hospitalized patients with rib fractures was calculated as 7%, and all the pneumonia diagnoses were made by an infectious diseases specialist. Therefore, we avoided the potential errors of studies reporting high pneumonia rates. It is also known in the literature that each additional rib fracture increases the rate of pneumonia development by 27% and the mortality rate by 19%.[3,8] In our study, the number of broken ribs was found to be an independent risk factor in multivariate analysis. In this respect, our study achieved similar results to the literature.

IGs occur in states of inflammation and infection.[9] Being able to detect IGs quickly can help diagnose many diseases early. They are a marker with successful results in diagnosing bacterial pneumonia, sepsis, acute pancreatitis, and acute appendicitis and predicting prognosis.[10-13] In our study, we observed the effect of IGs in a new area. Our study showed that they are effective in the early diagnosis of pneumonia developing secondary to thoracic trauma. If the IG number is greater than 0.06 in the sample taken at 48 hours, the risk of pneumonia increases 9.44 times. In addition, when the ROC curves in our study were examined, it was observed that the IG number at 48 hours gave excellent results in diagnosing pneumonia, with 75% sensitivity and 88% specificity (cut off: 0.055, AUC: 0.827, p=0.002).

In our study, the CRP value was statistically insignificant (p=0.373) in the diagnosis of pneumonia in multivariate analysis. CRP is a non-specific test. It is already known that

CRP is elevated in both trauma and pneumonia situations. Therefore, it has been observed that it cannot sufficiently help the diagnosis of pneumonia in trauma patients.

Our study may have some implications in clinical practice. In our study, it was shown that the risk of pneumonia increased in patients with WBC >12.000 and IG# >0.06 at 48$^{th}$ hour. The clinical reflection of this may be that in patients with rib fractures, it can be decided whether to start antibiotic therapy or not by simply looking at the 48$^{th}$ hour hemogram value.

### Limitations

The our study is that, it is a retrospective and single-center study. More studies are needed to generalize the results. In addition, rib fixation surgery could not be performed in our hospital at the time of the study. It is known that rib fixation reduces the incidence of pneumonia.[14] There was only one thoracic surgeon working in our hospital. On days when the thoracic surgeon was on leave, patients with thoracic trauma were transferred out of the province. This may have affected the results of the study.

## CONCLUSION

Our study showed that IGs are an effective marker in the early diagnosis of pneumonia secondary to rib fractures. Patients with an IG count greater than 0.06 at 48 hours have a 9.44-fold increased risk of pneumonia.

## ETHICAL DECLARATIONS

### Ethics Committee Approval

The study was carried out with the permission of Kastamonu University Clinical Researches Ethics Committee (Date: Decision No: 2022-KAEK-58).

### Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

### Referee Evaluation Process

Externally peer-reviewed.

### Conflict of Interest Statement

The authors have no conflicts of interest to declare.

### Financial Disclosure

The authors declared that this study has received no financial support.

### Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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