

Does the Percentage of Immature Granulocytes Predict the Severity and Mortality of the Disease in Patients with Acute Pancreatitis Presenting to the Emergency Department?

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Abstract

Objective: In this study, it was aimed to investigate the percentage of immature granulocytes (IG) and other hemogram parameters in the early period in predicting severe disease, in-hospital and short-term mortality in patients with acute pancreatitis (AP).

Materials and Methods: Our study was designed as a retrospective observational clinical study. Patients admitted to the emergency department with the diagnosis of AP between 01.01.2017 and 31.12.2021 years were included in the study. Hemogram parameters were compared according to mortality and the Balthazar severity index.

Results: We found that the percentage of IG was not statistically significant for mortality and disease severity. We found that the mean age of the group with mortality was statistically significantly higher than that of the group without mortality ($p=0.012$). We found that the lymphocyte count was statistically significantly lower in the group with mortality compared to the group without mortality. When we grouped the patients according to the Balthazar severity index, 366 (85.12%) of the patients were evaluated in the mild group, 61 (14.19%) in the moderate group, and 3 (0.69%) in the severe group. Among the groups; we found significant differences in hemoglobin, white blood cell (WBC), neutrophil, length of stay, and Balthazar severity index.

Conclusion: The IG percentage does not have a predictive value for the severity of the disease and the mortality process, particularly in patients with mild AP. A decrease in lymphocyte count can be considered a marker for mortality and long-term hospitalization. In patients with AP, WBC count and neutrophil count can be used to predict the severity of the disease on the first admission to the emergency department.

Keywords: Immature granulocyte, mortality, pancreatitis

Introduction

Acute pancreatitis (AP) is an acute inflammatory process of the pancreas and the mortality rate of the disease can vary between 3 and 17% depending on the severity of the disease and complications [1,2]. AP is inflammation caused by damage to the acinar cells of the exocrine pancreas. It is thought to result from the activation of early enzymes in the pancreas [3]. The severity of the disease can range from mild pancreatic edema to systemic inflammation leading to pancreatic necrosis, organ failure, and death [4].

Today, many classifications are used to determine the severity of the disease. There are many scorings such as Ranson criteria, the Accuracy of Acute Physiology and Chronic Health Evaluation II scoring, Bedside index of severity in AP scoring and Balthazar computed tomography (CT) scoring. However, these scores are still insufficient to predict the severity of the disease at the patient's first admission to the emergency department [5]. Therefore, the search for parameters that can predict serious disease in AP patients continues.



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Immature granulocytes (IG) are not normally found in the peripheral bloodstream. Recent studies have shown that IG are markers of inflammation in diseases such as sepsis, AP, and acute appendicitis [6-8].

However, studies on IG are limited. This study, was aimed to investigate the percentage of IG and other hemogram parameters in the early period in predicting severe disease, and in-hospital and short-term mortality in patients with AP.

Materials and Methods

Research Design

In the study, the data of patients who applied to the emergency department with the diagnosis of AP between 01.01.2017 and 31.12.2021 were recorded retrospectively from the hospital information management system. All patients over the age of 18 who were diagnosed with AP based on examination findings, laboratory tests and imaging methods in the emergency department were included in the study. The study was conducted by collecting data between 10.02.2022 and 10.04.2022. In the study, patients' age, gender, additional disease information, hemoglobin (Hgb), hematocrit level (Hct), white blood cell (WBC), neutrophil count, lymphocyte count, platelet count, imaging results [CT, ultrasonography (USG)], hospitalization information, length of hospitalization, clinical outcome, and short-term mortality information were recorded.

In the study, 542 AP patients admitted to the emergency department from January 2017 to the end of December 2021 were screened. Since recurrent pancreatitis could not be differentiated from chronic pancreatitis retrospectively, it was excluded in the study (Figure 1).

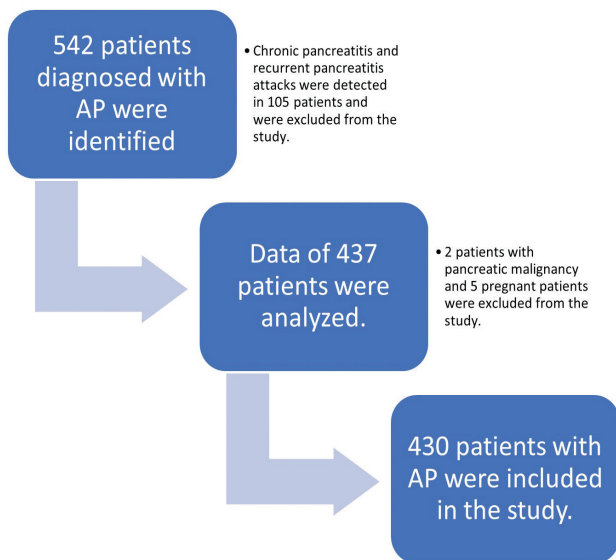


Figure 1. Flowchart of the cases included in the study

In the analysis of the data, the patients were divided into various groups. These groupings are as follows.

Patients with gallstones or biliary sludge detected by USG or CT were included in the biliary pancreatitis group, and patients without gallstones or biliary sludge were included in the non-biliary pancreatitis patient group. All the patients who were not discharged were included in the hospitalization group and compared with the discharged patients. Using the Balthazar CT severity index, patients were divided into three classes: Mild, moderate and severe pancreatitis. Patients with mortality within one month (detected by the E-nabız system and hospital information management system) were included in the mortality group, and patients without mortality within 1 month were included in the non-mortality group.

Exclusion Criteria

- Patients whose information cannot be accessed in the hospital information management system,
- Patients presenting with chronic and recurrent pancreatitis attack,
- Patients under 18 years of age,
- Patients with pancreatic malignancy,
- Pregnant patients,
- Patients with hematological diseases,
- Patients with a history of immunosuppression.

Statistical Analysis

The data obtained were analyzed in SPSS Statistics 24.0 (IBM Inc., New York, USA) program. Categorical data were presented as numbers and percentages. To test the normality of continuous variables, Kolmogorov-Smirnov and Shapiro-Wilk tests and skewness and kurtosis values were used. Data that fit the normal distribution were shown as the arithmetic mean and standard deviation and those that did not fit were shown as the median and interquartile range. Pearson chi-square and Fisher's Exact test were used in the analysis of categorical variables, and independent sample t-test and Mann-Whitney U test were used in the comparison of continuous variables. All statistical analysis were performed at the 95% confidence interval and values less than 0.05 were considered significant for the p value.

Results

A total of 430 patients, 260 (60.5%) women, and 170 (39.5%) men, were included in our study. Descriptive statistics of the study group are given in Table 1. Considering the distribution of the patients according to their clinical results, 261 (60.7%) patients were admitted to the service and 10 (2.3%) patients to the intensive care unit. One (0.2%) patient died in the emergency

Table 1. General characteristics of the research groups

		Non-biliary	Biliary	p
		n	n	
Gender	Woman	100	160	0.018
	Man	85	85	
Diabetes mellitus	Present	42	51	0.638
	Absent	143	194	
Hypertension	Present	47	75	0.236
	Absent	138	170	
Cholelithiasis	Present	22	27	0.778
	Absent	163	218	
Alcoholism	Present	2	1	0.396 ^a
	Absent	183	244	
Hyperlipidemia	Present	15	15	0.424
	Absent	170	230	
Malignancy	Present	3	5	0.523 ^a
	Absent	182	240	
Mortality	Present	1	6	0.121 ^a
	Absent	184	239	
Clinical outcome	Discharged	60	98	0.107
	Hospitalization	125	147	

^a: Fisher's Exact test

department and 158 (36.7%) patients were discharged from the emergency department. When the 1 month mortality of the patients was examined; we found that 7 (1.6%) patients died within 1 month and 423 (98.4%) patients did not experience mortality.

When we grouped the patients according to pancreatitis types; we found that the mean age of patients with biliary pancreatitis was statistically significantly higher than that of non-biliary patients ($p=0.013$). In patients with non-biliary pancreatitis, lymphocytes and length of hospital stay was statistically significantly higher than in patients with biliary pancreatitis. We found that platelet-lymphocyte ratio (PLR) values in patients with biliary pancreatitis were significantly higher than those in patients with non-biliary pancreatitis ($p<0.01$). We did not find a statistically significant difference in other parameters (Table 2).

When we grouped the patients according to their discharge status; we found that the Hgb, Hct, Balthazar score, WBC, neutrophil-lymphocyte ratio (NLR), and PLR values of the hospitalized patients were statistically significantly higher than the values of the discharged patients ($p<0.01$). Lymphocyte levels were statistically significantly higher in discharged patients compared in hospitalized patients ($p<0.01$). We did not find a statistically significant difference in other variables. In the grouping made according to mortality; we found that the mean age of the group with mortality was statistically

significantly higher than that of the group without mortality ($p=0.012$). We found that the lymphocyte value was statistically significantly lower in the group with mortality compared to the group without mortality ($p<0.01$). We did not find a statistically significant difference between the groups in any other parameters (Table 3).

When we grouped the patients according to the Balthazar severity index, 366 (85.12%) of the patients were evaluated in the mild group, 61 (14.19%) in the moderate group, and 3 (0.69%) in the severe group. In the analysis of intergroup variables; we found significant differences in Hgb, WBC, neutrophil, length of hospital stay, and Balthazar severity index. Since the number of patients in the severe group is insignificant, in the double group analysis made by adding it to the moderate severity group; we found significant differences in Hgb, WBC, neutrophil, length of hospital stay, and Balthazar severity index (Table 4).

Discussion

IG (including promyelocytes, myelocytes, and metamyelocytes) are early granulocytes released from the bone marrow during infection and inflammatory conditions. The presence of IG in peripheral blood indicates leukopoiesis and indicates infection, inflammation, and bone marrow stimulation. When leukocytes are used peripherally, the bone marrow produces more leukocytes in response. As a result, an "left upper shift"

Table 2. Analysis of variables by pancreatitis types

	Pancreatitis	Mean	SD	p value
Age	Non-biliary	54.95	17.54	0.013
	Biliary	59.34	18.69	
Hemoglobin	Non-biliary	13.48	1.96	0.050
	Biliary	13.10	1.97	
Hematocrit	Non-biliary	39.46	5.07	0.152
	Biliary	38.72	5.51	
Balthazar score	Non-biliary	1.63	1.47	0.301
	Biliary	1.48	1.51	
		Median	IQR	
White blood cell	Non-biliary	12110	6120	0.133
	Biliary	11325	5587.50	
IG %	Non-biliary	0.40	0.30	0.826
	Biliary	0.40	0.20	
Neutrophil	Non-biliary	9200	6600	0.516
	Biliary	9210	5422.50	
Lymphocyte	Non-biliary	1500	1200	<0.01
	Biliary	1200	1000	
Platelet	Non-biliary	245000	119000	0.396
	Biliary	261000	103500	
Neutrophil-lymphocyte ratio	Non-biliary	5.73	9.23	0.172
	Biliary	6.43	8.42	
Platelet-lymphocyte ratio	Non-biliary	154.62	144.19	<0.01
	Biliary	189.69	166.82	
Length of hospital stay (day)	Non-biliary	5.0	8.0	0.020
	Biliary	3.0	6.0	

Student's t-test, Mann-Whitney U test, SD: Standard deviation, IQR: Interquartile range, IG: Immature granulocytes

occurs. Although its predictive value in sepsis and many infections has been investigated recently, it is thought that it is not a sufficient parameter alone despite positive results. In our study, the percentage of IG was not found to be statistically significant for 1 month mortality, disease severity, and inpatient treatment. In a study by Çıldır and Kocaoğlu [9], IG % levels were found to be significantly higher in patients with severe AP, and in-hospital mortality. However, Doğan and Gürleyen [10] in research conducted in 2022, it was found that the percentage of IG in patients with acute perforated appendicitis was significantly higher than in patients without perforation. In a study conducted on patients with sepsis in 2019, Ayres et al. [11] found the IG percentage was significant in demonstrating sepsis. Jeon et al. [12] found that the percentage of IG was moderately significant in demonstrating sepsis in patients who developed sepsis after burns in 2021. Karon et al. [13] in 2017, found that the percentage of IG was moderately significant in showing sepsis in sepsis patients. Türkmen et al. [14] in 2022, the percentage of IG in sepsis patients was found to be higher in

the sepsis group than in the control group, and the difference was statistically significant. Ha et al. [15] in 2014, did not find the percentage of IG significant in demonstrating the 28 day mortality in sepsis patients. In our study, it was thought that the reason for the low IG % value was that most of our patients were patients with mild pancreatitis and that we could have caught patients in the early stages of leukopoiesis.

When we looked at the other hemogram parameters of AP patients, a relationship was found between the WBC count and neutrophil count and the severity of the disease in our study. Additionally, a relationship was found between lymphocyte count and mortality and length of hospital stay. In a study in which AP patients were divided into two according to the Ranson score; WBC, mean platelet volume, and NLR were found to be higher and statistically significant in the group with a high Ranson score, and the differences in PLR values were not statistically significant [16]. In a study by Keskin [17] in patients with AP in 2020, WBC, neutrophils, lymphocytes,

Table 3. Analysis of variables in clinical outcome and mortality status

	Clinical outcome	Mean	SD	p value	Mortality	Mean	SD	p value
Age	Discharged	56.78	17.30	0.552	Present	78.57	16.21	0.012
	Hospitalization	57.85	18.89		Absent	57.10	18.15	
Hemoglobin	Discharged	12.82	1.85	<0.01	Present	12.96	1.08	0.480
	Hospitalization	13.53	2.00		Absent	13.27	1.98	
Hematocrit	Discharged	37.93	5.11	<0.01	Present	38.90	3.49	0.921
	Hospitalization	39.68	5.35		Absent	39.04	5.36	
Balthazar score	Discharged	1.21	1.37	<0.01	Present	1.71	1.70	0.796
	Hospitalization	1.74	1.52		Absent	1.54	1.49	
		Median	IQR			Median	IQR	
WBC	Discharged	10610	5505	<0.01	Present	12530	5030	0.435
	Hospitalization	12220	5950		Absent	11515	5945	
IG %	Discharged	0.40	0.20	0.238	Present	0.50	0.30	0.418
	Hospitalization	0.40	0.30		Absent	0.40	0.30	
Neutrophil	Discharged	8060	5410	<0.01	Present	11410	5625	0.117
	Hospitalization	9960	6270		Absent	9100	579750	
Lymphocyte	Discharged	1600	1100	<0.01	Present	800	550	<0.01
	Hospitalization	1200	1000		Absent	1300	1075	
Platelet	Discharged	260500	103000	0.272	Present	229000	50500	0.199
	Hospitalization	249000	113000		Absent	254500	109500	
NLR	Discharged	4.66	4.99	<0.01	Present	14.51	14.64	<0.01
	Hospitalization	7.96	11.09		Absent	6.24	8.50	
PLR	Discharged	155.38	122.48	<0.01	Present	271.11	136.36	0.020
	Hospitalization	198.46	196.58		Absent	181.79	169.96	
Length of hospital stay (day)	Discharged			<0.01	Present	4.0	9.50	0.948
	Hospitalization	6.0	5.0		Absent	4.0	7.0	

Student's t-test, Mann-Whitney U test. SD: Standard deviation, IQR: Interquartile range, IG: Immature granulocytes, WBC: White blood cell, NLR: Neutrophil-lymphocyte ratio, PLR: Platelet-lymphocyte ratio

NLR, and PLR were found to be higher in severe pancreatitis. In a case-control study, the lymphocyte level was found to be statistically significantly lower in the patient group [18]. We think that the decrease in lymphocyte count is due to consumption due to the effect of inflammation. We believe that the decrease in lymphocyte count is associated with prolongation of hospital stay and mortality and can be used in the emergency room for the prognosis of the patient.

In studies showing the relationship between the female gender and AP; the rate of female patients was determined as 49.3%, 53%, and 57.5% [19,20]. In the study of Williams et al. [21], it was reported that the rate of female patients was 1.4 times higher than that of males. Biliary pancreatitis is the most common type of pancreatitis, although it varies regionally. Biliary pathologies are more common in female patients than in males, so a higher rate can be expected in female patients.

This relationship was considered the reason for the high rate of female patients in our study.

In previous studies in our literature review; biliary etiology was determined in different values such as 53.46%, 60.9%, 22.7%, and 80.9% in AP patients [22-25]. As seen in the literature, biliary tract pathologies were found to be the most common etiology in our study. Our study is also compatible with the literature.

In a study by Hayran [26] in 2015, 20% of the patients diagnosed with AP were discharged from the emergency department, 58% were hospitalized in the service and 22% were hospitalized in the intensive care unit. Bayındır [27] in a study conducted on 229 patients in 2018, it was stated that 98.7% of the patients were admitted to the ward and 1.3% of the patients were admitted to the intensive care unit. In the

Table 4. Analysis of variables with the Balthazar computed tomography severity index

	Mild (n=366)	Moderate (n=61)	Severe (n=3)	p	p ²
	Median (IQR) (minimum-maximum)				
Age	57.00 (28)	54.00 (31.5)	47.00 (23-54)	0.278	0.406
Hemoglobin	13.20 (2.60)	13.65 (2.40)	14.00 (13.10-16.10)	0.031	<0.01
Hematocrit	39.20 (6.50)	40.10 (6.25)	41.50 (38.0-48.20)	0.130	0.061
Balthazar CT severity index index	1 (2)	4 (0.0)	10	<0.01	<0.01
White blood cell	11395 (5810)	12495 (5765)	13140 (12800-16600)	<0.01	<0.01
IG %	0.40 (0.30)	0.40 (0.30)	0.40 (0.30-2.30)	0.887	0.781
Neutrophil	8775 (5590)	10215 (5760)	11160 (9800-13800)	<0.01*	<0.01*
Lymphocyte	1350 (1075)	1300 (1100)	1200 (900-2100)	0.996	0.968
Platelet	255500 (108500)	229000 (110500)	292000 (244000-803000)	0.254	0.469
NLR	6.05 (8.41)	8.33 (10.04)	11.50 (4.67-12.40)	0.248	0.104
PLR	180.71 (171.35)	185.85 (172.23)	271.11 (139.05-669.17)	0.563	0.881
Length of hospital stay (day)	4.0 (6.0)	7.0 (6.25)	0 (0-3.0)	<0.01	<0.01

*Kruskal-Wallis test, p²: Calculated for mild and moderate + severe groups, Mann-Whitney U test. IQR: Interquartile range, IG: Immature granulocytes, WBC: White blood cell, NLR: Neutrophil-lymphocyte ratio, PLR: Platelet-lymphocyte ratio, CT: Computed tomography

results of our study, we determined that most patients (63%) were planned for inpatient treatment, and this was consistent with the literature.

In an AP study by Aktaş [28] with 138 patients; mortality was observed in the 1 month period in 3.3% of the patients participating in the study. Knudsen et al. [29] in the Danish population, the 30 day mortality rate was 10% in 1988-1992, the 30 day mortality rate was 6.3% in 2013-2017, 4.2%, and 3.9% in the study of Miller et al. [30]. In the study of Yurt [22] it was reported as 7.2%. Our 30 day mortality rate was low compared to the literature. We believe that the inclusion of milder cases according to the Balthazar severity index resulted in a lower mortality rate.

Study Limitations

There are some limitations to our research: The most important of these limitations is the retrospective and single-center planning of the study. The information of the patients was obtained from the hospital electronic database and files in the hospital archive. The very unequal distribution of patient groups according to the Balthazar severity index can be counted as another limitation of the study.

Conclusion

The IG value does not have a predictive value for the severity of the disease and the mortality process in patients with AP. We think that leukocyte count, lymphocyte, and neutrophil count

are useful markers in predicting the severity of the disease in patients with AP at the first admission to the emergency department.

Ethics

Ethics Committee Approval: Ethics Committee of University of Health Sciences Turkey, İstanbul Kanuni Sultan Suleyman Training and Research Hospital (subject number: KAEK/2022.02.39).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: S.K., B.Y., Concept: S.K., S.D., Design: S.K., S.D., A.E., U.M.K., Data Collection or Processing: S.K., S.D., A.E., B.Y., U.M.K., Analysis or Interpretation: S.K., S.D., A.E., Literature Search: S.K., S.D., Writing: S.K., S.D., B.Y., U.M.K.

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