

ASSOCIATION OF CLINICAL AND EARLY ROUTINE LABORATORY FINDINGS WITH SEVERITY OF ACUTE PANCREATITIS

DOI: 10.36740/WLek202202104

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ABSTRACT

The aim: To identify the association of clinical and simple laboratory data determined during hospitalization of the patient with severity of acute pancreatitis.

Materials and methods: Clinical and laboratory parameters of 229 patients with acute pancreatitis were analyzed. All patients were divided into two groups depending on the severity of acute pancreatitis: in the group with mild AP were 130 (56.8%) patients and the group, which included moderately severe and severe degree of AP consisted of 99 (43.2%) patients.

Results: The association of the age group of 61-70 years with the severity of acute pancreatitis was revealed ($p < 0.05$). We did not find an association between the causes of acute pancreatitis and its severity. In the group with moderate-severe acute pancreatitis, the frequency of concomitant pathology was significantly higher than in the group with mild acute pancreatitis – 92.9% (92) and 78.5% (102) cases ($p < 0.05$). The association between the severity of acute pancreatitis and the following laboratory parameters: blood sugar, leukocyte levels, the level of stabs, lymphocytes, total protein, serum amylase, urinary diastase, creatinine, ALT, AST, prothrombin index, neutrophil-lymphocyte ratio was revealed ($p < 0.05$).

Conclusions: The study did not reveal a significant difference between compared groups in the time of hospitalization; found no association between the causes of acute pancreatitis and its severity. Instead, the association between female sex, the presence of concomitant pathology and some routine laboratory findings with the severity of acute pancreatitis was proved.

KEY WORDS: acute pancreatitis, severity, clinical data, laboratory data

Wiad Lek. 2022;75(2):351-356

INTRODUCTION

Acute pancreatitis (AP) is an acute inflammation of the pancreas with frequent involvement of peripancreatic tissue in the process. According to the Atlanta classification, there are three forms of its severity: mild, moderate and severe [1]. Mortality in acute pancreatitis is associated with the severity of its clinical course and ranges from 3.9% to 6% [2,3]. With moderate and severe acute pancreatitis, the mortality rate increases to 9.4%, and in case of joining the infection to the source of necrosis, the mortality rate reaches 30% [4,5].

The timeliness of the treatment of patients with acute pancreatitis significantly affects its effectiveness. An important task is the early diagnosis of its severe forms, especially at the stage of initial assessment of severity [6]. Predicting the severity and mortality of acute pancreatitis is an integral part of the treatment and diagnostic process, especially in the admission department, because it allows to quickly orient and determine the further treatment of the patient – in a surgical department or in the intensive care unit. The initial assessment of the severity of a patient with acute pancreatitis includes an assessment of both clinical and laboratory parameters. A large number of scales have been developed to assess the severity of acute pancreatitis and to predict mortality. Due to the variety of clinical and

morphological forms of acute pancreatitis there is a need to develop integrated scales with a comprehensive assessment of clinical, laboratory data and data of additional methods of examination – Ranson, APACHE II, SAPS, Glasgow-Imrie, MODS, SOFA [7,8].

The proposed clinical, laboratory markers of severity of acute pancreatitis and indicators of special methods of examination have different sensitivity and specificity, so they need further study to find the most sensitive indicators in the early period since the onset of disease [9]. Recent studies have shown a link between C-reactive protein, AST, creatinine and albumin and the severity of acute pancreatitis [10,11,12]. However, C-reactive protein reaches its diagnostic values only in 2-4 days, so it cannot be used to assess the severity of acute pancreatitis in the early stages of the process [13].

The variety of predictors of severity and mortality in acute pancreatitis has necessitated numerous studies. Laboratory relationships such as neutrophil-lymphocyte, platelet-lymphocyte ratios with the severity of acute pancreatitis, the duration of hospital stay and mortality in acute pancreatitis have also been shown [14]. In recent years, more and more publications have appeared about the predicting performance of red-cell distribution width, red-cell distribution width to total serum calcium ratio

and blood urea nitrogen for severity and mortality acute pancreatitis [15,16].

The literature we analyzed describes many prognostic clinical factors and laboratory markers that are related to the severity and mortality of acute pancreatitis. However, not all of them are early markers, developed for the specific capabilities of each clinic, some are quite expensive and impossible to use as obligatory in the emergency department at hospitalization of patients with acute pancreatitis. Therefore, today there is an active search for those early markers which can be possible to determine in an emergency hospital, taking into account the diagnostic and financial capabilities of medical establishment.

THE AIM

The aim of the study was to identify the association of clinical and simple laboratory data determined during hospitalization of the patient with the severity of acute pancreatitis.

MATERIALS AND METHODS

Clinical and laboratory parameters of 229 patients with acute pancreatitis who were hospitalized in the city clinical emergency hospital of Vinnytsia from 2018 to 2020 were analyzed. The age of patients ranged from 18 to 88 years. The mean age was 46.6 ± 14.7 years. Among the examined patients, there were 73 women (31.9%) and 156 men (68.1%), respectively.

The diagnosis of acute pancreatitis was made on the basis of the criteria recommended in the Atlanta 2012 classification, in the presence of any two of three criteria: characteristic abdominal pain (acute epigastric pain, often irradiating to the back), increased serum lipase / amylase levels (in 3 times and above the upper limit of normal), and appropriate findings on computed tomography, magnetic resonance imaging or transabdominal sonogram [1]. According to this classification, the severity of acute pancreatitis was distinguished between mild, moderate and severe, based on the presence of local and systemic complications, organ failure. Organ failure was determined using the criteria of a modified Marshall scoring system.

All patients with acute pancreatitis underwent a comprehensive clinical and laboratory examination, electrocardiography, chest X-ray, esophagogastroduodenoscopy, ultrasound examination of the abdominal cavity and retroperitoneal space, using Siemens Healthineers, ACUSON Juniper ultrasound scanner, for patients with severe acute pancreatitis computed tomography of the abdominal cavity was done, using Siemens Somatom go.up computer tomograph.

The following parameters were evaluated: age, sex, body mass index, etiology of acute pancreatitis, time from the onset of the disease to the moment of hospitalization, form of acute pancreatitis, concomitant pathology, complications of acute pancreatitis, hemoglobin in blood, blood sugar, leukocytes level with formula, erythrocytes,

hematocrit, ESR, total protein level, total bilirubin, serum amylase, urinary diastase, AST, ALT, urea, creatinine, prothrombin index, calculated the neutrophil-leukocyte ratio. The laboratory parameters, that were evaluated, were obtained at hospitalization.

All patients were divided into two groups depending on the degrees of severity of acute pancreatitis: the group with mild AP and the group, which combined moderately severe and severe degree of AP (we called it moderate-severe AP group). In the group with mild AP there were 130 (56.8%) patients with a mean age of 44.9 ± 14.4 years. The group with moderate-severe AP consisted of 99 (43.2%) patients with a mean age of 48.9 ± 14.9 ($p < 0.05$). The gender distribution of patients in groups was as follows: in the group of patients with mild AP there were 96 men (73.8%) and 34 (26.2%) women; in the group of patients with moderate-severe AP there were 60 men (60.6%) and 39 (39.4%) women respectively ($p < 0.05$). 174 (75.9%) patients had acute edematous type of AP, 55 (24.1%) patients had acute necrotising type of AP. The average hospital-stay in the group with a mild degree was $7,1 \pm 3,2$ day, in the group with moderate-severe was $15,4 \pm 8,2$ day.

All patients were analyzed for the time from the onset of the disease to the time of hospitalization. As the time of the onset of the disease was considered the appearance of abdominal pain.

The causes of acute pancreatitis were determined. In 151 (65.9%) patients the cause of pancreatitis was alimentary factor, in 43 (18.8%) patients was an alcohol factor, gallstone disease became the cause of AP in 17 (7.4%) patients. In addition, the causes of acute pancreatitis in 4 (1.7%) patients was taking medication for other diseases, in 2 (0.9%) cases acute pancreatitis developed after surgery, in 1 (0.4%) patient acute pancreatitis developed after falling from a height. In 31 (13.5%) patients it was not possible to determine the cause of AP.

Clinically significant comorbidity occurred in 194 (84.7%) patients with acute pancreatitis. Often there was a combination of several pathologies in one patient.

Complications of acute pancreatitis developed in 63 (63.6%) patients from moderate-severe group of AP and were absent in the group of patients with mild degree. Often the same patients had a combination of several complications.

Surgical treatment was performed in 28 (28.3%) patients from moderate-severe group of acute pancreatitis. Among all 28 surgical interventions, minimally invasive interventions were performed in 6 (21.4%) patients, open surgical interventions were performed in 22 (78.5%) patients with acute pancreatitis.

The overall mortality among 229 patients with acute pancreatitis was 21 (9.2%). Postoperative mortality was 25% (7).

RESULTS

Men predominated in the gender structure of all patients with acute pancreatitis. The ratio of women to men was 1

Table I. Distribution of patients with acute pancreatitis by severity and age

Age of patients with AP (n=229)	Group with mild AP (n=130)	Group with moderate-severe AP (n=99)	P
Age, years	44,9±14,4	48,9±14,9	0,04
21-30 years	20 (15,4%)	10 (10,1%)	ns
31-40 years	37 (28,5%)	23 (23,2%)	ns
41-50 years	33 (25,4%)	20 (20,2%)	ns
51-60 years	23 (17,7%)	21 (21,2%)	ns
61-70 years	9 (6,9%)	18 (18,2%)	0,009
over 70 years	8 (6,2%)	7 (7,1%)	ns

ns - not significant difference

Table II. Distribution of patients by severity and type of acute pancreatitis

Type of AP n=229	Group with mild AP (n=130)	Group with moderate-severe AP (n=99)	P
Edematous (interstitial)	130 (100%)	44 (44,4%)	<0,0001
Necrotic (aseptic)	0 (0)	43 (43,4%)	<0,0001
Necrotic (infected)	0 (0)	12 (12,1%)	0,0001

Table III. Distribution of patients with acute pancreatitis by severity and time from the onset of the disease to hospitalization

Time from the onset of the disease to hospitalization, hours (n=229)	Group with mild AP (n=130)	Group with moderate-severe AP (n=99)	P
Up to 6 hours	14 (10,8%)	13 (13,1%)	0,58
6-24 hours	41 (31,5%)	28 (28,3%)	0,59
24-48 hours	42 (32,3%)	29 (29,3%)	0,62
> 48 hours	33 (25,4%)	29 (29,3%)	0,53

Table IV. Distribution of patients with acute pancreatitis by severity and causes

The reason of AP (n=229)	Group with mild AP (n=130)	Group with moderate-severe AP (n=99)	P
Alimentary	85 (65,4%)	66 (66,7%)	0,83
Alcoholic	26 (20,0%)	17 (17,2%)	0,58
Biliary	7 (5,4%)	10 (10,1%)	0,17
Caused by drugs	2 (1,5%)	2 (2,0%)	0,78
Postoperative	1 (0,8%)	1 (1,0%)	0,84
Posttraumatic	1 (0,8%)	0 (0)	0,38
Of unknown etiology	8 (6,1%)	3(3,0%)	0,16

to 2.1 ($\chi^2 = 60.2$, $p < 0.0001$). There was a predominance of women in the group with severe acute pancreatitis compared with the number of women in the group with mild pancreatitis – 34 (26.2%) and 39 (39.4%), respectively ($p < 0.05$).

The mean age of patients in the group with moderate-severe AP was higher than the mean age in the group with mild AP ($p < 0.05$). A significant age difference between the compared groups was observed in the age group from 61 to 70 years ($p < 0.05$) (Table I).

The number of patients with edematous type of AP in the group with mild degree of severity dominated the analogical rate in the group with moderate-severe degree – 130

(100.0%) and 44 (44.4%) cases, respectively ($p < 0.0001$) (Table II).

The time from the onset of the disease to the time of hospitalization is especially important when it comes to severe degrees of acute pancreatitis with rapid progression of hemodynamic disorders and organ dysfunction. We noted low early (up to 6 hours) hospitalization of patients with acute pancreatitis – 27 (11.8%) patients in both groups. More than half of patients (61.1%) in both groups were hospitalized for 6 to 48 hours. However, we did not note a significant difference when comparing the terms of hospitalization between groups with mild and moderate-severe acute pancreatitis ($p > 0.05$) (Table III).

Table V. Distribution of patients with acute pancreatitis by severity and laboratory parameters

Laboratory indicator	Group with mild AP (n=130)	Group with moderate-severe AP (n=99)	P
Hemoglobin, g/L	141,0±16,6	142,7±25,5	0,55
Blood sugar, mmol/L	5,7±1,9	7,7±4,2	<0,0001
Erythrocytes, ×10 ¹² /L	4,7±0,6	4,5±0,8	0,18
Leukocytes, ×10 ⁹ /L	9,7±3,2	12,2±4,7	<0,0001
Stabs neutrophils, %	7,4±6,4	16,3±12,2	<0,0001
Segmented neutrophils, %	67,4±11,0	66,5±10,9	0,53
Lymphocytes, %	18,7±8,9	12,8±7,7	<0,0001
Monocytes, %	4,0±2,2	3,9±3,0	0,72
Neutrophil-lymphocyte ratio	5,5±4,1	10,8±10,0	<0,0001
Hematocrit (Hct)	47,5±5,3	45,4±10,9	0,38
ESR, mm/hour	17,0±2,7	20,8±3,4	0,11
Total protein, g/L	66,6±7,9	70,0±10,0	0,02
Total blood bilirubin, micromol/L	27,8±7,6	29,7±7,7	0,66
Serum amylase, units/L	332,4±29,3	949,1±47,7	<0,0001
Urinary diastase, units	1601,5±93,1	5242,7±102,3	<0,0001
ALT, units/L	50,5±11,5	71,1±8,3	<0,0001
AST, units/L	108,9±48,7	139,3±104,0	0,004
Serum urea, micromol/L	7,6±4,5	8,4±4,7	0,31
Creatinine, micromol/L	117,5±29,0	126,3±33,5	0,02
Prothrombin index, %	92,3±8,1	87,2±12,1	0,002

Among the causes of acute pancreatitis, alcohol abuse and fatty / fried foods dominated – 194 (84.7%) cases. Alcohol abuse was the main cause of acute pancreatitis in 38 (88.4%) men among 43. In women, the dominant cause of acute pancreatitis was gallstone disease. Thus, among 17 patients with acute biliary pancreatitis 13 (76,5%) were women. Together, alimentary, alcohol and biliary factors caused the development of acute pancreatitis in 211 (92.1%) patients. We did not note a significant difference in the etiological factor of acute pancreatitis between the comparison groups (Table IV).

Postoperative pancreatitis, which developed in 2 (0.9%) patients, deserves special attention. In one patient it occurred after splenectomy, in another patient it developed after left hemicolectomy for a tumor of the colon. The occurrence of postoperative pancreatitis has some difficulties for early diagnosis, because its clinical symptoms are superimposed on the early postoperative period with its characteristic postoperative pain, functional intestinal paresis, the introduction of nonsteroidal anti-inflammatory drugs. All this erases the clinical picture of postoperative pancreatitis and makes it unclear for diagnosis.

The presence of concomitant pathology undoubtedly affects the course of acute pancreatitis, exacerbates disorders of the systems and organs that are compromised by the underlying disease, and often becomes the reason for prolonging hospital stay. Among the comparison groups in the group with moderate-severe acute pancreatitis, the fre-

quency of concomitant pathology was significantly higher than in the group with mild acute pancreatitis – 92.9% (92) cases and 78.5% (102) cases, respectively ($p<0.05$). A significant predominance of the number of cases of concomitant pathology in the group of patients with moderate-severe AP compared with the group of patients with mild AP was observed in the following pathologies: diabetes mellitus – 12 (12.1%) and 5 (3.8%) ($p<0.05$); gallstone disease – 19 (19.2%) and 12 (9.2%), respectively ($p<0.05$); concomitant pathology of the stomach and duodenum – 67 (67.7%) and 58 (44.6%), respectively ($p<0.05$); obesity – 13 (13.1%) and 4 (3.1%), respectively ($p<0.05$).

The analysis of laboratory parameters determined during hospitalization of patients, revealed a significant difference in the comparison groups between the following indicators: blood sugar, leukocyte level, the level of stabs, lymphocytes, total protein, serum amylase, urinary diastase, ALT, AST, creatinine level, prothrombin index, neutrophil-lymphocyte ratio ($p<0,05$) (Table V).

In the structure of complications in patients from moderate-severe AP group transient organ failure and persistent organ failure developed in 63 (63.6%) cases, pleuritis – in 27 (27.3%) cases, fluid collections – in 16 (16.2%) cases, phlegmon of the retroperitoneal space in 11 (11.1%) cases, peritonitis – in 16 (16.2%) cases, pseudocyst of the pancreas – in 7 (7.1%), pancreatogenic diabetes mellitus – in 3 (3.0%) cases, parapancreatic abscess – in 1 (1.0%) case, other complications – in 34 (34.3%) cases.

DISCUSSION

In total, 29 early laboratory biomarkers for the severity in acute pancreatitis were reported in 181 studies [17]. In recent years at the stage of hospitalization much attention is paid to the study of hemogram as a simple and cost-effective method of outcome prediction in patients with acute pancreatitis [18]. In the current study, we have studied the association of almost 20 early routine laboratory indicators with severity of acute pancreatitis. The group of patients with moderate-severe acute pancreatitis has showed simultaneous significant increase in the level of enzymes in the blood and urine during hospitalization, which indicated the presence of active inflammation of the pancreas.

Changes in the general analysis of blood in patients with acute pancreatitis in the early phase of the disease are not strictly specific [9]. Related to this is the difficulty of differential diagnosis between aseptic and septic types of AP in early stage. In the group of patients with moderate-severe acute pancreatitis there was moderate leukocytosis – $12.2 \pm 4.7 \times 10^9 / L$, a shift of the leukocyte formula to the left – $16.3 \pm 12.2\%$ of stabs and a decrease of lymphocytes to $12.8 \pm 7.7\%$ compared with similar indicators in the group with mild acute pancreatitis ($p < 0.05$).

The significant relationship between stress hyperglycemia and adverse clinical outcomes in acute pancreatitis was proved [19]. The presence of hyperglycemia 7.7 ± 4.2 mmol/L in the group of patients with moderate-severe AP indicates an impression of the pancreatic parenchyma and is an unfavorable prognostic factor.

The prothrombin index in patients with moderately-severe AP was lower than in the mild group ($p < 0.05$), which can be explained by the development of hyper- and dys-metabolism syndrome, which is more expressed in severe types of AP.

In this study, there was a significant increase in the neutrophil-lymphocyte ratio (NLR) in the group of patients with moderate-severe AP compared with the same indicator in the group with mild degree ($p < 0.05$). The increase in NLR can be explained by the fact that in the presence of a powerful source of inflammation, the number of neutrophils increases. At the same time, severe impressions exhaust the immune system and reduce the number of lymphocytes [14]. Therefore, the higher the NLR, the more severe the patient's condition.

The overall mortality rate in acute pancreatitis is associated with its severity and increases with joining the infection to the source of necrosis [2-5,20]. In our study, there were no fatalities in the group of patients with mild AP. There were 21 deaths in the group of patients with moderate-severe AP, including 20 in patients with severe disease and 1 in patient with moderate disease. Among all patients, who died, 7 (33.3%) were operated on. Postoperative mortality was 25%.

CONCLUSIONS

1. Men predominated in the structure of all patients with acute pancreatitis, but there was a significant predomi-

nance of women in the group with severe AP compared with mild – 34 (26.2%) and 39 (39.4%), respectively ($p < 0.05$). The association of the age group of 61-70 years with the severity of acute pancreatitis was revealed ($p < 0.05$).

- Most often (61.1%) patients were hospitalized in the period from 6 to 48 hours from the onset of the disease. There was no significant difference between the terms of hospitalization in the groups of patients with mild and moderately-severe acute pancreatitis ($p > 0.05$).
- We did not find an association between the causes of acute pancreatitis and its severity. In both comparison groups, the dominant causes of AP were alimentary-alcohol and biliary factors – in 211 (92.1%) patients. There were gender differences in the structure of the causes of AP: alcohol abuse was the main cause of acute pancreatitis in men, in women the dominant cause was gallstone disease.
- In the group of patients with moderate-severe acute pancreatitis, the frequency of concomitant pathology was significantly higher than in the group with mild acute pancreatitis – 92.9% (92) cases and 78.5% (102) cases, respectively due to diabetes, gallstone disease, pathology of the stomach and duodenum and obesity ($p < 0.05$).
- The association between the severity of acute pancreatitis and the following laboratory parameters determined during hospitalization of patients: blood sugar, leukocyte levels, the level of stabs, lymphocytes, total protein, serum amylase, urinary diastase, creatinine, ALT, AST, prothrombin index, neutrophil-lymphocyte ratio was revealed ($p < 0.05$).

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Conflict of interest:

The Authors declare no conflict of interest.

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Received: 12.04.2021

Accepted: 28.08.2021

A – Work concept and design, **B** – Data collection and analysis, **C** – Responsibility for statistical analysis,

D – Writing the article, **E** – Critical review, **F** – Final approval of the article