Original article

Running title: Clinical and laboratory data associated with mortality from pancreatitis

Clinical and Simple Laboratory Data Associated with Fatal Outcomes in Patients with Acute Pancreatitis

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SUMMARY

Aims. The aim of the study was to evaluate the association of mortality in acute pancreatitis with clinical and simple laboratory data received on the day of admission.

Patients and methods. In our retrospective study, the clinical and laboratory parameters of 99 patients with moderate and severe acute pancreatitis were analyzed. All patients were divided into two groups: deceased and survivors.

Results. We did not find a significant difference in age and gender distribution between the comparison groups. However, a significant predominance of alcoholic etiology of acute pancreatitis, early hospitalization (up to 6 hours from the onset of the disease) of patients, and the number of necrotizing infected type in the deceased group were found. Concomitant pathology did not significantly differ in comparison groups. In patients from the deceased group, the total number of all complications was significantly higher than in the group of survivors – 21 (100%) and 42 (53.8%) (p = 0.0001), respecting. Among the laboratory parameters determined on the day of admission, in the deceased group, there was a significant increase in stabs to 19.8 ± 9.8 and ESR, AST to 225.3 ± 47.5 U/L, urea to 11.2 ± 7.7 mmol/L, and creatinine to 173.6 ± 26.1 mmol/L.

Conclusion. The alcoholic genesis of acute pancreatitis, necrotizing infected type of inflammation of the pancreas, presence of late complications, and comorbidities were significantly higher in the deceased group. The levels of stabs, ESR, AST, urea, and creatinine determined on the admission significantly dominated in the deceased group, which requires further study for the prediction of mortality of acute pancreatitis.

Keywords: acute pancreatitis, mortality, clinical data, simple laboratory data

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INTRODUCTION

Acute pancreatitis remains an urgent problem of the modern medicine. Total mortality in acute pancreatitis is ranging from 3.9% to 9.7% (1, 2). Mortality in severe acute pancreatitis is significantly higher and reaches up to 30% in patients with infected necrosis (3, 4).

Predicting the severity and mortality of acute pancreatitis remains a challenge. Many prognostic scales and markers of severity and mortality of acute pancreatitis have been proposed (5, 6). They all differ in sensitivity of the proposed markers. Many of various predictive scoring systems are limited in use because of the complexity of their daily clinical implementation (7, 8). In recent years, there has been a tendency to reduce the use of complex scales and move to more simplified scales. It is important to combine high predictive power, simplicity and rapid determination of these indicators, especially at the stage of admission department, when it is necessary to immediately determine the need for patient's hospitalization to intensive care unit and to substantiate treatment tactic and the infusion therapy regimen (9).

That is why in recent years more and more works appear aimed at finding simple, less invasive, cost-effective, short-term and quickly tested markers with broad availability in emergency departments (9). It is suggested to use hemogram-based markers, which are simple, objective, dynamic and readily available, in addition to conventional multifactorial scoring systems for prediction of outcome of acute pancreatitis (7). In particular, the prognostic value of the use of white blood count, blood creatinine level, AST level, hematocrit, blood urea nitrogen, C-reactive protein, albumin-bilirubin score, cell distribution width, neutrophil-lymphocyte ratio, lymphocyte-monocyte ratio and platelet lymphocyte ratio in predicting mortality and severity in patients with acute pancreatitis were described (10 - 13).

Thus, in recent years there has been an active search for early, effective and inexpensive markers. Clinical and laboratory test, which are easy to perform with hight predictive power are necessary, in addition to classical prognostic markers.

PATIENTS AND METHODS

Clinical and simple laboratory parameters of 99 patients with moderate and severe acute pancreatitis were analyzed retrospectively. All patients were treated in the surgical or intensive care unit of the Vinnytsia clinical city emergency hospital from January 2018 to December 2020. Inclusion criteria were patients with the diagnosis of acute pancreatitis, which was made according to the Atlanta classification 2012 in the presence of any two of the following three symptoms: characteristic abdominal pain, elevation of serum lipase/amylase three times higher than normal, and corresponding changes in the pancreas on imaging at CT or ultrasound. Pancreatitis severity was classified using the Revised Atlanta classification (14). Collection and processing of clinical and laboratory material was carried out in compliance with all ethical principles of the Declaration of Helsinki.

Determination of clinical and laboratory parameters was performed on the day of admission. Determination of complications and type of treatment was performed on the day of discharge. The data were entered into a specially designed database with subsequent data processing. Records of clinical patients' data included: sex, age, type of acute pancreatitis, etiology, severity, the time interval between onset of abdominal pain and admission to the hospital, comorbidity, complications of acute pancreatitis and type of treatment. Records of laboratory parameters, determined on the day of hospitalization, included: hemoglobin, blood sugar level, erythrocytes, leukocytes with the formula, hematocrit, ESR, total protein, total bilirubin, serum amylase, urinary diastase, alanine aminotransferase (ALT), aspartate transaminase (AST), urea, creatinine, prothrombin index, neutrophil-lymphocyte ratio. All patients with moderate and severe pancreatitis were required to perform visualization of the pancreas and abdominal organs by ultrasound and contrast-enhanced computed tomography.

All 99 patients with moderate and severe acute pancreatitis were divided into two groups depending on clinical outcomes: deceased group and group of those who survived on discharge moment. A survivors group included 78 (78.8%) cases, where-as the deceased group included 21 (21.2%) cases. The mean age of all patients with moderate and severe acute pancreatitis enrolled in this study was 48.9 \pm 14.9 years, with no significant difference between groups. The youngest patient from the deceased group was 25 years old, the oldest – 68 years old. There was a slight male predominance in the survivors group – 62.8% (49/99) (p > 0.05).

Treatment of patients with acute pancreatitis included infusion therapy and was performed depending on the severity of the disease in the surgical department or, in case of a need, an aggressive infusion therapy, epidural catheter placement, oxygen support and other intensive care - in the intensive care unit. Surgical treatment was required in 28.3% (28/99) cases with a slight predominance in the deceased group - 38.1% (8/21) compared to the group of survivors - 25.6% (20/78) (p > 0.05). In determining the surgical tactics for acute pancreatitis, modern paradigms of maximum delay of surgical intervention to the so-called "cold period" and the use of minimally invasive interventions as a "stepup" or final approaches were maintained. Among the 99 analyzed cases, open surgery was performed in 22 (22.2%) patients, minimally invasive - in 6 (6.1%) patients.

We evaluated the association between each clinical and laboratory parameter described above between patients with moderate and severe acute pancreatitis from deceased group and from the group of survivors on discharge. For statistical processing, all quantitative values were presented as Mean \pm SD. The significance of the percentage difference between the groups was calculated by the criterion χ^2 , and the mean values (Mean) by the T-test for independent samples by groups. The STATISTICA for Windows 10 was used. The significant level was considered p < 0.05.

RESULTS

Among all 99 patients with moderate and severe pancreatitis, the largest number of patients was in the age group 31-40 years – 23.2% (23/99). We did not find a significant difference in age and gender distribution between the comparison groups. However, a significant predominance of alcoholic etiology of acute pancreatitis in the deceased group was found – 47.6% (10/21). In the group of survivors, the alimentary etiology significantly prevailed – 71.8% (56/78). Most of patients from both groups were hospitalized into the hospital in the period 24-48 hours – 29.3% (29/99). The group of deceased patients was dominated by early hospitalization (up

Table 1. Comparison of groups by age, gender distribution, etiology and time from the onset of the disease to hospitalization

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Clinical data	Deceased group	Survivors group	P-value	
(n = 99)	(n = 21)	(n = 78)		
Age, years 48.9 ± 14.9	49.2±11.5	48.8 ± 15.8	ns	
21-30 years	1 (4.8%)	9 (11.5%)	ns	
31-40 years	5 (23.8%)	18 (23.1%)	ns	
41-50 years	5 (23.8%)	15 (19.2%)	ns	
51-60 years	5 (23.8%)	16 (20.5%)	ns	
61-70 years	5 (23.8%)	13 (16.7%)	ns	
Over 70 years	0 (0)	7 (9.0%)	ns	
Men, n = 60 (60.6%)	11 (52.4%)	49 (62.8%)	ns	
C	Genesis of acute pa	ncreatitis		
Alimentary	10 (47.6%)	56 (71.8%)	0.0003	
Alcoholic	10 (47.6%)	7 (8.9%)	< 0.0001	
Biliary	0 (0)	10 (12.8%)	ns	
Caused by drugs	0 (0)	2 (2.6%)	ns	
Postoperative	0 (0)	1 (1.3%)	ns	
Of unknown etiology	1 (4.8%)	2(2.6%)	ns	
Time from the onset of the disease to hospitalization				
Up to 6 hours	7 (33.3%)	7 (9.0%)	0,02	
6-24 hours	5 (23.8%)	23 (29.5%)	ns	
24-48 hours	4 (19.1%)	25 (32.0%)	ns	
> 48 hours	5 (23.8%)	23 (29.5%)	ns	

ns - not significant difference

Clinical data (n = 99)	Deceased group (n = 21)	Survivors group (n = 78)	P-value		
Types of acute pancreatitis					
Edematous (interstitial)	1 (4.8%)	41 (52.6%)	0.0001		
Necrotising:	20 (95.2%)	37 (47.4%)	0.0001		
- aseptic	11 (52.3%)	33 (42.3%)	ns		
- infected	9 (42.9%)	4 (5.1%)	< 0.0001		
Concomitant pathology					
Clinically significant comorbidity	21 (100%)	73 (93.6%)	ns		
Concomitant cardiovascular system pathology	12 (57.1%)	46 (59.0%)	ns		
Concomitant diabetes mellitus	3 (14.3%)	9 (11.5%)	ns		
Concomitant hepato-biliary system pathology	2 (9.5%)	17 (21.8%)	ns		
Concomitant pathology of the stomach and duodenum	2 (9.5%)	32 (41.0%)	0.007		
Another concomitant pathology	7 (33.3%)	21 (26.9%)	ns		
Concomitant obesity	5 (23.8%)	8 (10.3%)	ns		

Table 2. Comparison of groups by the type of acute pancreattis and comorbidity

ns - not significant difference

to 6 hours from the onset of the disease) than the group of survivors - 7 (33.3%) vs 7 (9.0%) (p < 0.05) (Table 1).

In the group of the deceased, 95.2% (20/21) patients developed necrotising pancreatitis, one patient (4.8%) developed interstitial oedematous pancreatitis. In the group of surviving patients, more than half of all patients - 52.6% (41/78) had interstitial oedematous type of acute pancreatitis. The number of necrotising cases in the group of deceased significantly exceeded the number of similar forms in the group of survivors – 95.2% (20/21) vs 47.4% (37/78) (p = 0.0001). Significant dominance of the infected necrotising type was especially noted in the group of deceased in comparison with the group of survivors – 42.9%(9/21) vs 5.1%(4/78) (p < 0.0001).

Concomitant pathology was present in almost all patients and did not differ significantly between the group of deceased and the group of survivors – 100% (21/21) and 93.6% (73/78) cases (p > 0.05), respectively. The structure of concomitant pathology in both groups was predominantly represented by pathology of the cardiovascular system (mainly coronary heart disease and hypertension), obesity and diabetes mellitus (Table 2).

All patients from the deceased group had complications of acute pancreatitis. In patients from

the group of survivors, the number of complications of acute pancreatitis was significantly lower – 21 (100%) and 42 (53.8%), respectively (p = 0.0001). The structure of complications in both groups of patients was dominated by early complications – 61.9% (13/21) and 38.5% (30/78) of cases, respectively. Late complications of acute pancreatitis in the group of deceased developed in 8 (38.1%) cases and were significantly higher than in the group of survivors with 12 (15.4%) analogous cases (p < 0.05) (Table 3).

Among the laboratory parameters determined on the day of admission, in the deceased group there was a significant increase in stabs up to $19.8 \pm 9.8\%$ compared with the group of survivors – $15.4 \pm 8.7\%$ (p < 0.05) and ESR – 26,3 ± 6,4 mm/hour compared with 19.9 ± 5.2 mm/hour (p < 0.0001). The levels of serum amylase and urine diastase were increased in both groups. There was a dissociation between these indicators: at almost the same level of serum amylase in both groups, the level of urine diastase in the deceased group was significantly lower than in the group of survivors and amounted to 3562.1 ± 108.9 units compared with 5680.2 ± 173.1 units (p < 0.0001). In both groups, there was an increase in liver enzymes ALT and AST with a significant predominance of ALT in the group of deceased in compar-

Clinical data	Deceased group	Survivors group	D 1		
(n = 99)	(n = 21)	(n = 78)	P-value		
Complications of acute pancreatitis					
Present complications:	21 (100%)	42 (53.8%)	0.0001		
-Early complications	13 (61.9%)	30 (38.5%)	0.05		
-Late complications	8 (38.1%)	12 (15.4%)	0.02		
Fluid collections	2 (9.5%)	14 (17.9%)	ns		
Phlegmon of the	5 (23.8%)	6 (7.7%)	0.04		
retroperitoneal space Parapancreatic abscess	1 (4.8%)	0 (0)	0.05		
Pancreatogenic type II diabetes mellitus	2 (9.5%)	1 (1.3%)	0.05		
Peritonitis	11 (52.4%)	5 (6.4%)	<0.0001		
Pancretic pseudocyst	0 (0)	7 (9.0%)	ns		
Pleuritis	11 (52.4%)	16 (20.5%)	0.004		
Other complications	21 (100%)	13 (16.7%)	<0.0001		
Oligoanuria / anuria	9 (42.9%)	7 (9.0%)	0.0002		

Table 3. Comparison of groups by the complications

ns - not significant difference

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Labortory data	Deceased group	Survivors group	P-value		
(n = 99)	(n = 21)	(n = 78)			
Laboratory indicators on the day of admission					
Hemoglobin, g/L	137.1 ± 30.8	144.2 ± 23.9	ns		
Blood sugar, mmol/L	8.7 ± 4.8	7.4 ± 4.0	ns		
Erythrocytes, ×10 ¹² /L	4.2 ± 1.1	4.6 ± 0.7	ns		
Leukocytes, ×10 ⁹ /L	12.2 ± 3.3	12.3 ± 5.1	ns		
Stabs neutrophils, %	19.8 ± 9.8	15.4 ± 8.7	0.03		
Segmented neutrophils, %	65.1 ± 13.0	66.9 ± 10.3	ns		
Lymphocytes, %	11.1 ± 6.8	13.2 ± 7.9	ns		
Monocytes, %	2.8 ± 1.1	4.2 ± 1.3	< 0.0001		
Neutrophil-lymphocite ratio	11.6 ± 5.7	10.6±6.1	ns		
Hematocrit (Hct)	45.8 ± 10.5	45.3 ± 8.9	ns		
ESR, mm/hour	26.3 ± 6.4	19.9 ± 5.2	< 0.0001		
Total protein, g/L	69.6±11.0	70.1±9.7	ns		
Total blood bilirubin, micromol/L	24.8 ± 10.8	31.2 ± 8.6	0.007		
Serum amylase, U/L	947.3 ± 55.0	949.8±40.4	ns		
Urinary diastase,un.	3562.1 ± 108.9	5680.2 ± 173.1	< 0.0001		
ALT, U/L	49.3 ± 8.2	79.3 ± 6.9	< 0.0001		
AST, U/L	225.3 ± 47.5	110.7 ± 67.4	< 0.0001		
Serum urea, mmol/L	11.2 ± 7.7	7.5 ± 2.8	0.02		
Creatinine, micromol/L	173.6 ± 26.1	109.5 ± 17.9	< 0.0001		
Prothrombin index, %	78.4 ± 14.1	90.0 ± 10.1	0.0003		

Table 4. Comparison of groups by the laboratory data

ns - not significant difference

ison with survivors group – 225.3 \pm 47.5 U/ L and 110.7 \pm 67.4 U/ L, respectively (p < 0,0001).

Elevations in urea and creatinine as a manifestation of early renal failure were significantly higher in the deceased group than in the group of survivors and amounted to $11.2 \pm 7.7 \text{ mmol/L}$ compared with $7.5 \pm 2.8 \text{ mmol/L}$ (p < 0, 05) and $173.6 \pm 26.1 \text{ mkmol/L}$ compared with $109.5 \pm 17.9 \text{ mkmol/L}$ (p < 0.0001). There were changes in the blood coagulation system, in particular the decrease in the prothrombin index in the group of deceased to $78.4 \pm 14.1\%$, compared with the same indicator in the group of survivors $90.0 \pm 10.1\%$ (p < 0,05) (Table 4).

DISCUSSION

Acute pancreatitis certainly remains an urgent problem of emergency surgery. The peak incidence in both groups occurred in the age range from 31 to 40 years – 23.2% (23/99) of cases, the predominant part of patients with acute pancreatitis are people of working age, so the problem is not only medical but also socio-economic.

We did not find significant gender differences between the groups. It should be noted that in both groups there was a slight predominance of men. The dominant etiological factor among the deceased patients was the alcohol factor - 47.6% (10/21) of cases, among the survivors the dominant factor was alimentary - 71.8% (56/78), which were often combined together. Therefore, we consider that according to the data of our study, the dominant etiological factor of acute pancreatitis in both groups was the alimentary-alcoholic factor. We want to note that one patient developed acute pancreatitis in the postoperative period as a result of surgical trauma, characterized by blurred clinical symptoms in the early postoperative period and the difficulty of diagnosis, which may be related to the application of nonsteroid unti-inflammatory drugs for multimodal analgesia of postoperative pain. Obviously, this type of pancreatitis needs further study.

Necrosis of the parenchyma of the pancreas and peripancreatic tissues worsens the course of acute pancreatitis and is accompanied by much higher mortality than its edema. In the group of deceased only, 1 (4.8%) of 21 patients had an interstitial oedematous type of acute pancreatitis, the remaining 20 (95.2%) of deceased patients had a necrotising type.

Late hospitalization of patients from the onset of the disease in both groups was the cause of dete-

rioration of the pathological process, the development of deep inflammatory systemic reactions with dysfunction of vital organs and systems. The presence of concomitant pathology, which was present in all deceased patients (100%) and in the majority of surviving patients (93.6%), was the reason for the exhaustion of the compensatory capabilities of organs and systems and development of their insufficiency.

Early complications of acute pancreatitis, which are the result of cytokine release and are often accompanied by hemodynamic disorders, have become dominant in both groups. The structure of complications in the group of deceased was dominated by enzymatic pleurisy – 11 (52.4%) cases, peritonitis – 11 (52.4%) and acute renal failure – 9 (42.9%) cases. In the group of survivors, complications developed only in one half of the patients and were represented mainly by enzymatic pleurisy – 16 (20.5%) cases and fluid accumulations – 14 (17.9%) cases. We did not find differences between the groups depending on the number and type of surgical treatment.

Analyzing the data of laboratory parameters in the groups, determined on the day of admission, we revealed a number of statistical differences between some of them. In particular, in the group of deceased there was a significant increase in indicators of inflammation: the level of stabs to 19.8 \pm 9.8% and ESR to 26.3 ± 6.4 mm/h; liver markers – increase in the level of AST to 225.3 ± 47.5 U/L; urea – up to 11.2 ± 7.7 mmol/L, creatinine – up to $173.6 \pm$ 26.1 mkmol/L, as a result of acute kidney injury. A slight increase in total bilirubin in both groups was noticed, which we regarded as the result of some compression of the terminal part of the common bile duct by the head of pancreas, which might be enlarged due to edema. There was an increase in the level of leukocytes and glucose in both groups, serum amylase, which had no statistical difference between the groups.

The calculation of the neutrophil-lymphocyte ratio was performed. It was proved earlier that this indicator, elevated during the first 48 h of admission, is significantly associated with severe acute pancreatitis and is an independent negative prognostic indicator in acute pancreatitis with the optimal cut-off 10.6 (day 0) (15). In our study, there was a significant increase in the neutrophil-lymphocyte ratio in both groups of patients without significant differences between groups: in the group of deceased, the neutrophil-lymphocyte ratio on the day of hospitalization was 11.6 \pm 5.7, and in the group of survivors – 10.6 \pm 6.1.

CONCLUSION

We did not reveal a significant difference in the age of patients and the gender distribution between the comparison groups. There was a significantly higher number of early hospitalizations (up to 6 hours) in the group of the deceased. Alcoholic genesis of acute pancreatitis, necrotising infected type of inflammation, the presence of complications and comorbidities were significantly higher in the group of deceased than in the group of survivors. The levels of stabs, ESR, AST, urea, creatinine determined on the day of admission were significantly higher in the group of the deceased.

Our study was conducted in one center and was based on the analysis of simple clinical and laboratory data, which were mostly determined on the day of admission in the patients with acute pancreatitis to the emergency department. The question of finding clinical and simple, affordable laboratory factors, predicting mortality in moderate and severe acute pancreatitis, remains relevant. Repeating it with multi-center involvement studies and with multivariable analyzes may be beneficial to obtain more reliable data. However, we believe that this report would be helpful for extracting useful data among the numerous factors related to the mortality of acute pancreatitis.

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Article info

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Kliničke i osnovne laboratorijske analize povezane sa fatalnim ishodom kod bolesnika sa akutnim pankreatitisom

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SAŽETAK

Cilj. Cilj ove studije bila je procena povezanosti mortaliteta kod akutnog pankreatitisa sa kliničkim i osnovnim laboratorijskim analizama urađenim na dan prijema bolesnika.

Metode. U našoj retrospektivnoj studiji analizirani su kliniči i laboratorijski parametri 99 bolesnika sa umerenim i teškim akutnim pankreatitisom. Svi pacijenti su podeljeni u dve grupe: preminuli i preživeli.

Rezultati. Nije pronađena značajna razlika u distribuciji starosti i pola između upoređivanih grupa. Međutim, u grupi preminulih preovladavale je značajna etiologija alkoholozma kod akutnog pankreatitisa, rana hospitalizacija bolesnika (do 6 sati od pojave bolesti), kao i nekrotizirajući infektivni tip. Udružena patologija nije se značajno razlikovala između upoređivanih grupa. Kod bolesnika iz grupe preminulih, ukupan broj komplikacija bio je značano veći nego u grupi preživelih: 21 (100%) i 42 (53,8%) (p = 0,0001). Među laboratorijskim parametrima dobijenim na dan prijema, u grupi preminulih utrđeno je značajno povećanje nezrelih neutrofila na 19,8 ± 9,8, doke su vrednosti ESR i AST iznosile 225,3 ± 47,5 U/L, uree 11,2 ± 7,7, i kreatinina 173,6 ± 26,1 mkmol/L.

Zaključak. Etiologija alkoholozma kod akutnog pankreatitisa, nekrotizirajući infektivni tip upale pankreasa, prisustvo kasnih konplikacija, kao i komorbiditeti bili su značajno povećani u grupi bolesnika koji su premunuli. Nivoi nezrelih neutrofila, ESR, AST i kreatinina određenih na dan prijema bili su značajni u grupi preminulih, što ukazuje na neophodnost daljeg ispitivanja predikcije mortaliteta kod akutnog pankreatitisa.

Ključne reči: akutni pankreatitis, mortalitet, klinički podaci, osnovne laboratorijske analize