SEVERITY PROGNOSTIC FACTORS IN ACUTE PANCREATITIS IN THE NATIONAL HOSPITAL SERGIO E. BERNALES

FACTORES PRONÓSTICOS DE SEVERIDAD EN PANCREATITIS AGUDA EN EL HOSPITAL NACIONAL SERGIO E. BERNALES

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ABSTRACT

Objective: To determine the prognostic factors of severity in patients with acute pancreatitis (AP) at the Hospital Nacional Sergio E. Bernales during the period June 2016 to June 2018. **Methods:** Study of cases and controls, being the cases patients with AP moderately severe or severe and controls those of mild AP. The medical records were reviewed to apply the APACHE-II score. Chi-square was used and the ORs were obtained with their respective 95% CI. SPSS 25 program was used. **Results:** 162 medical records were reviewed. 54 (33.3%) patients developed AP moderately severe or severe and 108 (66.7%) had mild AP. Of the patients with AP moderately severe or severe, 55.6% were men; while in mild AP the female sex was predominant with 91.7%. The majority were of biliary origin (83.3%). There was a predominance of mild AP. AP moderately severe or severe was associated with being over 60 years old (OR: 3.10; 95% CI: 1.26-7.65; p= 0.011), presenting pleural effusion (OR: 7.78 95% CI: 5.745-54.418 ; p <0.001), hematocrit>40% (OR: 4.17; 95% CI: 2.07-8.39; p <0.001) and APACHE score ≥8 (OR: 7.88; 95% CI: 3.77-16.45; p<0.001). **Conclusion:** The factors associated with the severity of pancreatitis were age, presenting pleural effusion, hematocrit> 40% and APACHE score ≥8.

Key words: Pancreatitis; APACHE; Prognosis. (source: MeSH NLM)

RESUMEN

Objetivo: Determinar los factores pronósticos de severidad en pacientes con pancreatitis aguda (PA) en el Hospital Nacional Sergio E. Bernales durante el periodo junio 2016 a junio 2018. **Métodos:** Estudio de casos y controles, siendo los casos los pacientes con pancreatitis moderada o severa y los controles los de pancreatitis leve. Los datos para las variables evaluadas fueron obtenidos a partir de la revisión de Historias Clínicas. Se usó chi-cuadrado para evaluar la asociación y se hallaron los OR con sus respectivos IC 95%. Se utilizó programa SPSS 25. **Resultados:** Se revisaron 162 historias clínicas de los cuales 54 (33,3%) pacientes desarrollaron PA moderadamente severa (PAMS) o severa (PAS) y 108 (66.7%) cursaron con PA leve (PAL). De las PAMS y PAS 55,6% fueron hombres; mientras que en las PA leves el sexo femenino fue el predominante con un 91,7 %. La mayoría fue de origen biliar con un 83,3%. Los factores asociados a PAMS/PAS incluyeron tener más de 60 años (OR: 3.10; IC 95%: 1,26-7,65; p= 0.011), presentar derrame pleural (OR: 7,78 IC 95%: 5,745-54,418; p<0.001), hematocrito >40% (OR: 4,17; IC 95%: 2.07-8.39; valor p: <0.001) y puntuación APACHE ≥8 (OR: 7,88; IC 95%: 3.77-16.45; p<0,001). **Conclusión:** Los factores asociados a severidad de la pancreatitis fueron la edad, presentar derrame pleural, hematocrito >40% y puntuación APACHE ≥8.

Palabras clave: Pancreatitis; APACHE; Pronóstico. (fuente: DeCS BIREME)

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INTRODUCTION

Acute pancreatitis (AP) is one of the most common gastrointestinal disorders that require hospitalization. Most of them are mild and self-limited, 30% are moderately severe and 10% are severe. Organ failure (OF) is the main gravity determinant and cause of early death. Overall mortality is 3-6% and increases to 30% in severe AP. Secondary infections, including infected ANP and sepsis, are responsible of more deaths in the last years[4].

Acute pancreatitis worldwide incidence has increased steadily, and ranges from 4.9 to 73.4 cases for each 100 000 inhabitants worldwide. Regarding Latin America, there was reported an incidence of 15.9 cases for each 100 000 inhabitants in Brazil, in 2006; a 3% incidence in Mexico in 2001 and an incidence of 28 cases for each 100 000 inhabitants, according to the statistics from Ministry for Health of Peru in 2009. Biliary etiology is primarily responsible for almost 70% of every case registered[5].

In a 2013 revision of the Atlanta classification, pancreatitis is categorized in mild, if there are neither organ failure nor local or systemic complications; moderate, if there is a transitory organ failure (lower than 48 hours) or systemic or local complications with no organ failure; and severe, if there is a persistent organ failure, which could be unique or multiple.[6] Although patients with severe AP represent a small proportion of patient with AP, these show a major morbidity and mortality, require special management and access to an Intensive Care Unit[7]. Being able to predict this severity may help us identify patients with increased risk of morbidity and mortality[5].

Severity can be predicted using clinical, laboratory and radiological parameters, severity indices and serum markers. Many of them can be obtained at the moment or within 48 hours. Nonetheless, the best predictor must be fast, reproducible, minimally invasive and accurate, especially for predicting patients with increased risk of death[8].

There has been a development of many scoring systems for the purpose of predicting the course of acute pancreatitis. For example, Ranson, APACHE II, BISAP, etc. which reach acceptable degrees of sensibility and specificity, but take more than 24 hours to be completed.

The main utility of prognostic systems are: to detect severe cases early, to select patients to assign treatment, to refer patients to specialized centers, to compare patients between different series and to recruit patients for new treatments[12].

Consequently, the need and importance to early and properly know and detect the severity prognostic factors in patients with AP will allow us carry an early and correct management in terms of these kind of patients, avoiding a great impact in their morbidity and mortality.

The main objective of this study is to determine severity prognostic factors in patients with acute pancreatitis (AP) in the National Hospital Sergio E. Bernales.

METHODS

Retrospective, observational, analytical, quantitative, case-control study.

We worked with patients diagnosed with acute pancreatitis in the gastroenterology service of the National Hospital Sergio E. Bernales from June 2016 until June 2018, who were classified in 2 study groups according to disease severity: patients with moderately severe and severe acute pancreatitis (cases); patients with mild acute pancreatitis (controls).

Data collection technique used was documentation, due to the use of secondary sources. That is to say, we reviewed medical records of every patient diagnosed with acute pancreatitis.

A data collection sheet was used as an instrument, which recorded the following information: epidemiological data (age, sex); clinical data (etiology, nutritional status, and pleural effusion); laboratory data (glucose and hematocrit level) and clinical-laboratory data (APACHE-II).

A database was created in the statistical program SPSS version 25, where was carried out a quality control of registers through consistence, compilation and re-categorization, providing a database without inaccurate or missing data and the ability to correct inaccuracies in data input and collection. We found OR with their correspondents confidence intervals at 95%.

RESULTS

We reviewed 162 medical records with a diagnostic of acute pancreatitis, the cases were 54 (33.3%) patients who developed moderately severe AP (MSAP) or severe AP (SAP) and the controls, 108 (66.7%) presented mild AP. Clinical features can be observed in Table 1.

Table 1. Clinical features of study population.

	Pancreatitis severity		Total
	MSAP and SAP	**Mild AP**	
Sex			
Female	24 (44,4%)	99 (91,7%)	123 (75,9%)
Male	30 (55,6%)	9 (8,3%)	39 (24,1%)
Etiology			
Biliary	35 (64,8%)	100 (92,6%)	135 (83,3%)
Alcoholic	17 (31,5%)	2 (1,9%)	19 (11,7%)
Other causes	2 (3,7%)	6 (5,6%)	8 (4,9%)

Regarding table 1 about clinical features of 162 patients, we obtained that 30 (55.6%) of MSAP and SAP were male; while female prevailed in terms of mild AP with 99 (91.7%) patients. Regarding etiology displayed on table 2, we found that 135 patients (83.3%) were of biliary etiology, 19 (11.7%) of alcoholic etiology and 8 patients (4.9%) presented other causes. Concerning MSAP and SAP, 35 (64.8%) were of biliary etiology. Amongst mild AP, it prevailed the same etiology.

Table 2. Bivariate analysis of severity prognostic factors of acute pancreatitis.

	Severity of pancreatitis		OR (CI 95%)	p value
	MSAP and SAP	**Mild AP**		
Age				
≥60 años	13 (24,1%)	10 (9,3%)	3,10 (1,26 – 7,65)	0,011
<60 años	41 (75,9%)	98 (90,7%)		
BMI				
≥25 kg/m2	39 (72,2%)	60 (55,6%)	2,08 (1,02 – 4,21)	0,040
<25 kg/m2	15 (27,8%)	48 (44,4%)		
Glycaemia				
≥200 mg/dl	10 (18,5%)	9 (8,3%)	2,50 (0,95 – 6,58)	0,058
<200 mg/dl	44 (81,5%)	99 (91,7%)		
Pleural effusion				
Yes	40 (74,1%)	29 (26,9%)	7,78 (3,70 – 16,35)	*0,001
No	14 (25,9%)	79 (73,1%)		
Hematocrit				
≥40%	37 (68,5%)	37 (34,3%)	4,17 (2,07 – 8,39)	*0,001
<40%	17 (31,5%)	71 (65,7%)		
APACHE score				
≥8 points	38 (70,4%)	25 (23,1%)	7,88 (3,77 – 16,45)	*0,001
<8 points	16 (29,6%)	83 (76,9%)		

PAMS: Moderately severe acute pancreatitis, PAS: Severe acute pancreatitis; Mild PA: Mild acute pancreatitis.

In table 2, the bivariate analysis shows that patients over 60 were 3.1 times more likely to develop MSAP and SAP, in contrast with patients under this age (OR: 3.10; CI 95%: 1.26-7.65; p value: 0.011).

Patients with overweight and obesity (BMI ≥25 kg/m2) are 2.08 times more likely to develop MSAP and SAP in comparison to those who got a BMI <25 (OR: 2.08; CI 95%:1.02-4.21; valor p: 0.040).

Regarding patients who developed MSAP and SAP, 74.1% of them showed pleural effusion, with an OR of 7.78 and a p value <0.001.

When it comes to patients with hematocrit >40%, they were 4.17 times more likely to develop MSAP and SAP, in contrast to those who got hematocrit <40% (OR: 4.17; CI 95%: 2.07-8.39; p value: <0.001).

In the matter of Apache score of ≥8 marks, we noted that patients were 7.88 times more likely to show disease severity in comparison with those who got a score of <8 (OR: 7.88; CI 95%: 3.77-16.45; p value:<0,001). The variable with which there was not statistically non-significant association was glycaemia's ≥200 mg/dl.

Table 3. Multivariate analysis of severity prognostic factors of acute pancreatitis.

Variables	Adjusted OR	CI 95%	p value
Age	0,735	(0,202-2,679)	0,641
BMI	7,153	(2,150-23,801)	0,001
Pleural effusion	17,682	(5,745-54,418)	0,001
Hematocrit	4,220	(1,593-11,180)	0,004
APACHE	25,064	(7,341-85,576)	<0,001

For the multivariate analysis displayed on table 4, we carried out a binary logistic regression analysis with the results obtained in the bivariate analysis, considering statistically significant variables.

The severity prognostic factors in patients with acute pancreatitis during the period from June 2016 until June 2018 were BMI ≥25 kg/m2 (p=0.001), pleural effusion (p=<0.001), hematocrit (p=<0.001) and apache ≥8 points (p=<0.001), all these factors with statistically significant values.

DISCUSSION

In this research, regarding epidemiological characteristics in patients with acute pancreatitis, we found that 33.3% of patients developed moderately severe acute pancreatitis (MSAP) or severe (SAP). Ocampo et al found similar studies with mild AP of 83.6% and severe AP of 16.4%[2], in 2015. Likewise in 2012, Enrique Madaria mentions in his study that 39.1% developed severe AP[29]. These numbers cannot be compared with Molina's research in 2013, which concluded that 82.4% corresponded to severe acute pancreatitis.[30]

Regarding the relationship between severity and sex, Molina obtained that female (53%) prevailed in

terms of acute pancreatitis, in general. Nonetheless, concerning severe acute pancreatitis, it was male sex (53.6%) 30 who prevailed. In our research, we found that 55.6% of MSAP and SAP were from male; while female sex prevailed regarding mild AP with 91.7%.

In relation to the etiology of acute pancreatitis, 83.3% were of biliary origin, 11.7% alcoholic and 4.9% had other causes. Gompertz et al noted that the most frequent etiology of AP was biliary, reaching 80-100% of causes in some hospitals in Ecuador and Peru, and 45-60% in Chile, Argentina and Brazil1. Alcohol consumption was an etiologic factor in 10-20%, with a similar number of cases considered idiopathic1. Ocampo et al name a similar result with 88.2% of biliary etiology as the main cause of acute pancreatitis[2].

Concerning the relationship between disease severity and etiology, we obtained that 64.8% of MSAP and SAP were of biliary etiology. Amongst mild AP, it prevailed the same etiology. These findings agree with Molina, who found that the main cause of acute pancreatitis, in both mild and severe, was a biliary process with a proportion over 80%[30].

In a 2011 research carried out by Chavarría et al, at National Hospital Cayetano Heredia, they found that

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APACHE II score with a cut-off point of 8 presented 9.02 times more likelihood to show disease severity with a p value under 0.01, in contrast to the group who showed the mild form.[9] This agrees with our study's findings, where we noted that an apache of ≥8 points apache represents 7.88 times the likelihood to develop severe acute pancreatitis, in comparison with those who got an apache of <8 points (OR: 7.88; CI 95%: 3.77-16.45; p value:<0.001). Jin et al, in 2017, proved that an APACHE II score of ≥ 8 was a risk factor for developing moderately severe AP or severe AP with an OR of 29.096 and a p value of <0.00133. Furthermore, we carried out the multivariate analysis of statistically significant variables. There we could note related results to our research with an OR of 25.064 and a p value of <0.001. Thus, proving to be a useful predictor for discerning between both groups in our environment.

Pacheco et al, in 2009, reported that acute pancreatitis severity was influenced by age (OR: 1.02; IC 95%: 1.01–1.04, p value: 0.001)[15]. Our research does not agree, however, with the previous result. We carried out a multivariate analysis to every bivariate analysis' statistically significant variable, but we did not found statistical significance in age >60 years old as a severity prognostic factor (OR: 0.735, CI 95%: 0.202-2.679; p value: 0.641). In a research by Roulin et al in 2018, we found similar results. There was no difference regarding clinical and radiological severity of acute pancreatitis between elderly and young people (p value: 0.210).[19]

In our research, a BMI ≥25 kg/m2 was statistically significant (OR: 2.08; CI 95%:1.02-4.21; p value: 0.040). Many published studies support this argument, since obesity is one of the most significant severity negative prognostic factors and increases both risk of local and systemic complications. According to Fei Y et al in 2017, univariate analysis confirmed that BMI Is significantly related to severity of AP with an OR of 0.917; IC 95%: 0.682-1.733, valor p: 0.01120. Likewise, in a study published at National Hospital Daniel Alcides Carrión by Guzmán in 2012, 14 out of 16 patients with severe pancreatitis got a BMI > 25. (p = 0.03; OR = 4.39)25. The relationship between obesity and development of severe acute pancreatitis is due to the fact that obese patients have a chronic proinflammatory state, which may predispose them to a major inflammatory response if they develop acute pancreatitis. The hypothesis that supports this evidence comes from two studies that show an increase in both protein C and proinflammatory cytokines levels (IL-1b, IL-6 e IL8) in obese patients with acute pancreatitis in comparison with non-obese patients.[25]

Regarding blood glucose level, we did not found any statistical significance in our study (OR: 2.50; CI95%: 0.95-6.58; p value: 0.058), even though a study by Speranskaya in 2015 reports that blood glucose >200 after being admitted to the hospital is related with severity degree of pancreatitis (p<0.001).[21] More studies are need in order to reaffirm these findings and to observe if a better glycaemia control while being admitted to the hospital influences in the hospital evolution of pancreatitis.

Hematocrit has been described in a number of studies as a possible severity marker in acute pancreatitis. Pathophysiologically, in severe cases it exists a redistribution of intravascular fluid towards a third space as a consequence of inflammatory process due to the initiation of inflammatory cascade, which joins a local process after an increase of pancreatic enzymes' release. Thus, detection of this reduction in the intravascular volume could be related to disease severity. Chavarría et al (2001) state in their research that hematocrit average value in the group labeled as mild was 38.40%, whereas in the group of severe patients this average was 39.78% with p value: 0.182. Thus, it was a non-significant difference9. However, in our study we obtained that patients who got hematocrit >40% were 4.17 times more likely to develop MSAP and SAP, unlike those who got hematocrit <40% (OR: 4.17; CI 95%: 2.07-8.39; p value: <0.001). Likewise, Sánchez in 2015 proved hematocrit to be a great predictor of acute pancreatitis severity with p value of 0.012.[34]

Presence of pleural effusion, an easy-to-prove mark, has been reported as a proper prognostic factor in various scientific papers. Nevertheless, in these papers presence of pleural effusion was researched through different radiological methods and within heterogeneous population with different etiologies in their pancreatitis. Also, in those papers, there is no comparison between predictive accuracy of presence of pleural effusion and prognostic systems of traditional multi-criteria. In our study, we obtained the following as a result of bivariate analysis: OR of 7.78 with a CI 95% between 3.70-16.35 y and p value of <0.001. This result is similar to the study published by Ocampo et al (2008), where evaluated pleural effusion through echography presented higher values of predictive accuracy in predicting systemic complications (OR: 6.3 CI95%: 2.85-14)[23]. Further, León C. (2015) found in his research work that 100% of patients with severe pancreatitis presented pleural effusion.[35]

CONCLUSION

In our study we established that pleural effusion is more frequent in patients with severe acute pancreatitis and together with the APACHE scale they were significantly associated, being the best predictors of disease severity.

Authorship Contributions: The authors participated in the genesis of the idea, project design, data collection and interpretation, analysis of results and preparation of the manuscript of this research paper.

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