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Factors associated with hospital length of stay in children with acute pancreatitis☆,☆☆

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KEYWORDS
Acute pancreatitis;
Children;
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Abstract
Introduction and aim: Acute pancreatitis (AP) is the most common cause of pancreatic disease in children. Previous studies have described factors related to days of hospital length of stay (LOS) in children. Our aim was to identify factors associated with LOS in AP.
Materials and methods: A retrospective study was conducted at the *Hospital Infantil de México Federico Gómez* in Mexico City, encompassing the time frame of January 1, 2017 and March 31, 2019. AP was confirmed by medical chart review, according to the INSPPIRE criteria at the time of hospital admission, in patients below 18 years of age. AP grade was classified, following the NASPGHAN guidelines. Demographic, clinical, biochemical, nutritional, and treatment data were collected. Prolonged hospital LOS was considered that which lasted 7 days or longer.
Results: Fifty-one events (32 patients) were registered. Median LOS was 8 days (IQR 4–14 days). Antibiotic use was significantly associated with longer LOS (OR 31.71; 95% CI: 2.71–370.65; $p = 0.006$) and early feeding (EF) (within 72 h of admission) was associated with shorter LOS (OR 0.05; 95% CI: 0.001–0.63; $p = 0.02$). There was no association between LOS and the variables of age, recurrence, grade, etiology, comorbidities, complications, fluid resuscitation, parenteral nutrition, or biochemical characteristics upon admission.
Conclusion: Our study, like others, corroborated the fact that EF in the management of AP was associated with fewer days of hospital LOS.

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PALABRAS CLAVE
Pancreatitis aguda;
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Nutrición enteral;
Estancia hospitalaria

Factores asociados con estancia hospitalaria en niños con pancreatitis aguda

Resumen
Introducción y objetivo: La pancreatitis aguda (PA) es la causa más común de enfermedad pancreática en niños. Estudios previos exponen factores relacionados con los días de estancia hospitalaria (EH) en niños. Nuestro objetivo fue identificar factores asociados con EH en PA.
Material y métodos: Se realizó un estudio retrospectivo en el Hospital Infantil de México Federico Gómez de la Ciudad de México, del 1 de enero de 2017 al 31 de marzo de 2019. Se confirmó PA por revisión del expediente clínico, de acuerdo con los criterios INSPPIRE en pacientes menores de 18 años de edad al tiempo de su admisión. El grado de PA se clasificó de acuerdo con los lineamientos de la NASPGHAN. Se recabó información demográfica, clínica, bioquímica, nutricional y de tratamiento. Se consideró estancia hospitalaria prolongada (EHP) aquella mayor o igual a 7 días.
Resultados: Se registraron 51 eventos (32 pacientes). La mediana de EH fue de 8 días (RIQ 4–14 días). El uso de antibióticos estuvo asociado significativamente con una mayor EH (RM 31.71; IC 95%: 2.71–370.65; p = 0.006) y la alimentación temprana (AT) (dentro de 72 horas del ingreso) se asoció con una disminución de EH (RM 0.05; IC 95%: 0.001-0.63; p = 0.02). No se encontró asociación entre edad, recurrencia, grado, etiología, comorbilidades, complicaciones, reanimación hídrica, uso de nutrición parenteral y características bioquímicas al ingreso y EH.
Conclusión: En nuestro estudio, como en algunos otros, se corrobora que, en el manejo de la PA, la AT está asociada con una disminución de los días de EH.

Introduction and aim

Acute pancreatitis (AP) is the most common cause of pancreatic disease in children. Its incidence has increased worldwide in the last two decades and is estimated at 3.6–13.2 cases per 100,000 children[1,2]. There is evidence that the number of cases has been rising in Mexico in recent years[3]. The etiology of AP varies at the different hospital centers, but the most common causes are those of biliary, anatomic, and genetic origin; up to 20% of cases are idiopathic[3–5]. AP is responsible for $200 million USD in hospital expenses, with a median hospitalization cost of $20,000 USD[6]. Studies conducted on children show different factors associated with days of hospital length of stay (LOS), that include: chronic illnesses (oncologic, gastrointestinal, neurologic, hematologic), parenteral nutrition (PN), Hispanic ethnicity, pseudocyst or pancreatic necrosis, malnutrition, male sex, disease severity, systemic inflammatory response syndrome (SIRS), comorbidities, and fasting time[6–8].

The European Society for Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) recently published guidelines for the treatment of AP in children, in addition to nutritional recommendations that support starting early enteral nutrition (EN), reserving the use of PN for severe cases, and administering antibiotics only in cases of infected necrosis[9,10].

The aim of the present study was to identify factors associated with LOS in pediatric patients hospitalized for AP at a tertiary care hospital in Mexico City, Mexico.

Materials and methods

Study design

A retrospective study was conducted that reviewed the medical records of patients discharged from the different hospitalization departments (General Pediatrics, Gastroenterology and Nutrition, Cardiology, Internal Medicine, Emergencies, Intensive Care) of the *Hospital Infantil de México Federico Gómez* in Mexico City, Mexico, within the time frame of January 1, 2017 and March 31, 2019, under the International Classification of Diseases 10th edition, (ICD-10) code K85.9 for AP, according to the retrospective study sheet. AP diagnosis was confirmed, in conformity with the ***In**ternational **S**tudy group of **P**ediatric **P**ancreatitis: **I**n search for a cur**e*** (INSPPIRE) criteria:[11] a) abdominal pain consistent with AP, b) amylase and/or lipase levels three-times higher than the upper limit of normal, and c) imaging consistent with AP, in patients under 18 years of age at admission. The exclusion criteria were patients with pancreatic tumors and patients that developed AP during their hospitalization due to other diagnoses.

Data collection

The demographic and clinical variables were collected (the latter including symptoms, grade, number of events, etiology, comorbidities, medication use, complications, deaths, and imaging studies), along with the biochemical parameters (lipase, amylase, cholesterol, C-HDL, C-LDL, triglycerides, creatinine, blood urea nitrogen [BUN], total

bilirubin [TB], direct bilirubin, indirect bilirubin, aspartate aminotransferase [AST], alanine aminotransferase [ALT], albumin, glucose, gamma-glutamyl transpeptidase, hemoglobin [Hb], hematocrit [Hct], leukocytes, platelets, calcium, and lactate dehydrogenase [LDH]), anthropometric parameters (weight, height, body mass index), treatment established (fluid resuscitation, pain management, nutritional therapy, antibiotics, and PN). Early feeding (EF) was defined as oral or enteral feeding begun within the first 72 h of hospitalization. Comorbidities (dyslipidemia, type 1 diabetes mellitus, obesity, pancreas divisum, psychiatric disorder, gallstones, recurrent pancreatitis, inflammatory bowel disease, hepatitis, chronic kidney disease, DiGeorge syndrome, sickle cell disease, parathyroid hyperplasia, cystic fibrosis, celiac disease) and complications, such as imaging findings suggestive of chronic pancreatitis/chronic pancreatic injury (whether ductal changes: irregular main pancreatic duct, intraductal filling defect, stones, stricture or dilation; or changes in the parenchyma: focal/generalized enlargement, cavities, calcifications, heterogeneous echotexture), exocrine pancreatic insufficiency (identified through fecal elastase test <100 μg/g of stools or fat determination in stools <90% collected over 72 h), and endocrine pancreatic insufficiency (diagnosis of diabetes mellitus), according to the NASPGHAN definitions of pancreatitis in children, were also registered. The classification of complications (local or systemic) and the grade of pancreatitis (mild, moderately severe, severe) were categorized in accordance with the guidelines of the NASPGHAN Pancreas Committee[12].

Statistical analysis

Descriptive statistics were utilized to jointly present the data of the entire study group. The nominal variables were expressed as percentage. The type of distribution of the quantitative variables was determined through the Kolmogorov–Smirnov test. The numerical variables with normal distribution were expressed as mean $\pm$ standard deviation (SD) and the variables with free distribution were expressed as median with interquartile range (IQR). Grouping the patients according to hospital LOS (prolonged LOS [PLOS] was considered that which was equal to or greater than 7 days), a bivariate analysis was carried out, in which all the variables were compared. The Student's t test was utilized to compare the quantitative variables that had normal distribution and the Mann–Whitney U test for those that did not. The nominal variables were compared using the chi-square test or the Fisher's exact probability test.

The association of the variables with the outcome was carried out through a univariate analysis, with the odds ratio (OR) calculation and a 95% confidence interval (95% CI). A multiple logistic regression model was employed to control the effects of the confounding factors, in which all the variables that showed a $p \leq 0.20$ in the multivariate analysis were taken into account. Statistical significance was set at a $p < 0.05$. The data were analyzed with the SPSS version 20.0 for Windows (IBM Corp., Armonk, NY) program.

Ethical considerations

Because clinical records were reviewed, authorization by the Ethics Committee was not required, nor was informed consent needed from the patients analyzed, given that no personal information that could identify them was contained in the study.

Results

Fifty-one events of AP were registered, corresponding to 32 patients that met the selection criteria. Half of the events occurred in females (51%, n = 26/51). The median age at diagnosis was 11.5 years (IQR 7.8–14.3 years). A total of 68.2% of the cases had recurrence. Seventy-eight percent of the events involved abdominal pain, accompanied by vomiting in 49% (n = 25/51) and isolated abdominal pain without vomiting in 29.4% (n = 15/51). A total of 62.7% (n = 32/51) of the events were considered mild, 29.4% (n = 15/51) moderately severe, and 7.8% (n = 4/51) severe. Anatomic/obstructive etiology (pancreas divisum, annular pancreas, accessory pancreatic duct, cholelithiasis, biliary sludge, choledochal cyst) was the most frequent (58.8%, n = 30/51) and the remaining causes were: idiopathic (17.6%, n = 9/51), traumatic (9.8%, n = 5/51), toxic (9.8%, n = 5/51), and metabolic/toxic (3.9%, n = 2/51). Comorbidities were not registered in 27.4% (14/51) of the patients; 14 (27.4%) patients had recurrent pancreatitis; the combination of annular pancreas/recurrence and pancreas divisum/recurrence presented in 6 and 3 patients, respectively. Likewise, 6 (11.7%) patients presented with obesity (4/51 with recurrence and 2/51 as an isolated event). A total of 62.7% (n = 32/51) of the patients presented with no complications (local or systemic), pancreatic cyst or pseudocyst was documented in 19.6% (n = 10/51), 2 (3.9%) patients presented with pancreatic necrosis, one (2%) patient had an isolated peripancreatic collection, and the rest of the events (n = 6, 11.7%) involved combinations of the abovementioned, plus organ failure (kidney, heart, lung) or SIRS. The median hospital LOS was 8 days (IQR 4–14 days), and the mean hospital LOS was 11.76 $\pm$ 13.45 days.

Initially, only 21.5% (n = 11/51) of the patients received fluid resuscitation with Ringer's lactate solution (RL). For pain management, 49% (n = 25/51) of the cases received opioids and non-opioids, together, whereas 29.4% (n = 15/51) received non-opioids and 13.7% (n = 7/51) received opioids. Antibiotics were indicated for and administered to 49% (n = 25/51) of the cases.

Fasting was indicated for all the patients upon hospital admission. Thirty-two (62.7%) episodes were managed with EF (23 patients with mild AP, 8 with moderately severe AP, and only one patient classified as severe AP). Subdividing the 32 admissions that received EF, 21 received it within the first 48 h of admission (17 with mild AP and 4 with moderately severe AP) and 11 between >48 h and <72 h from admission (6 with mild AP, 4 with moderately severe AP, and 1 with severe AP). Clear liquid diet was the most frequently indicated (76.4%, n = 39/51), followed by normal diet (15.6%, n = 8/51), and administration was oral in 92.1% (47/51). The registers of nutrient proportions or the caloric supply administered were not available. PN was indicated in 10 patients

Table 1 Bivariate analysis of the demographic and clinical characteristics by type of hospital stay.

n	With PLOS 27	Without PLOS 24	p
Age (years)	9.99 ± 4.67	11.76 ± 4.01	0.15[a]
Sex			
Male, n (%)	12 (44.4%)	13 (54.2%)	0.48[b]
Female, n (%)	15 (55.6%)	11 (45.8%)	
Weight (kg)	34.08 ± 18.16	38.17 ± 17.04	0.41[a]
Height (cm)	132.9 ± 26.72	140.85 ± 23.84	0.26[a]
BMI	17.7 ± 4.18	18.3 ± 4.23	0.63[a]
Recurrence (2 or more events), n (%)	13 (48.2%)	19 (79.2%)	0.02[b]
Grade			
Mild, n (%)	10 (37 %)	22 (91.7%)	0.001[b]
Moderately severe, n (%)	13 (48.2%)	2 (8.3%)	
Severe, n (%)	4 (14.8%)	0	
Etiology			
Anatomic (n:12)/obstructive (n:18), n (%)[c]	12 (44.4%)	18 (75%)	0.07[b]
Idiopathic, n (%)	6 (22.2%)	3 (12.5%)	
Traumatic, n (%)	2 (7.4%)	3 (12.5%)	
Toxic, n (%)	5 (18.5%)	0	
Metabolic/toxic, n (%)	2 (7.4%)	0	
Presence of comorbidities, n (%)[d]	16 (59.3%)	21 (87.5%)	0.03[b]
Presence of complications, n (%)	5 (18.5%)	12 (50%)	0.02[b]
Chronic injury	7 (75%)	12 (100%)	0.25[b]
Endocrine pancreatic insufficiency	1 (25%)	0	0.25[b]

BMI: body mass index; PLOS: prolonged length of stay.
[a] Student's t test.
[b] Chi-square test.
[c] Anatomic: pancreas divisum (n = 5), annular pancreas (n = 6), accessory pancreatic duct (n = 1); Obstructive: cholelithiasis (n = 9), biliary sludge (n = 6), choledochal cyst (n = 2), post-endoscopic retrograde cholangiopancreatography (n = 1).
[d] Comorbidities: recurrent pancreatitis (n = 14), annular pancreas/recurrent pancreatitis (n = 6), obesity/recurrent pancreatitis (n = 4); cholelithiasis/recurrent pancreatitis (n = 4), pancreas divisum/recurrent pancreatitis (n = 3); obesity (n = 2), cholelithiasis (n = 2), dyslipidemia (n = 1), obesity/cholelithiasis/dyslipidemia (n = 1).

Table 2 Bivariate analysis of the biochemical characteristics upon admission by type of hospital stay.

n	With PLOS 27	Without PLOS 24	p
Lipase U/l	1634.5 (673.5–5134.7)	3331 (1139–5442)	0.22[a]
Amylase U/l	232.5 (102–959.25)	271 (152.5–785.5)	0.71[a]
Creatinine mg/dl	0.69 ± 0.34	0.58 ± 0.20	0.14[b]
BUN mg/dl	19.93 ± 20.51	11.56 ± 5.19	0.05[b]
Total bilirubin mg/dl	1.71 ± 1.59	0.58 ± 0.30	0.001[b]
AST U/l	73.5 (22.5–185.75)	21 (16–28)	0.02[a]
ALT U/l	95 (28.5–201.5)	25 (18–29)	0.03[a]
Albumin mg/dl	3.26 ± 0.86	4.08 ± 0.47	0.0001[b]
Hb g/dl	13.12 ± 2.56	14.24 ± 1.85	0.08[b]
Hct %	39.45 ± 7.63	42.36 ± 5.61	0.13[b]
Leukocytes $10^3/\mu l$	12.12 ± 7.48	11.89 ± 4.60	0.89[b]
Platelets $10^3/\mu l$	250.31 ± 130.38	319.0 ± 93.67	0.04[b]
Calcium mg/dl	8.98 ± 0.81	9.32 ± 0.51	0.07[b]
LDH U/l	396 (232–479)	215 (172.5–303.5)	0.008[a]

ALT: alanine aminotransferase; AST: aspartate aminotransferase; BUN: blood urea nitrogen; Hb: hemoglobin; Hct: hematocrit; LDH: lactate dehydrogenase; PLOS: prolonged length of stay.
[a] Mann–Whitney U test.
[b] Student's t test.

Table 3 Bivariate analysis of the treatment characteristics by type of hospital stay.

n	With PLOS 27	Without PLOS 24	p
Fluid resuscitation, n (%)	11 (40.7%)	0	0.0001[a]
Pain management, n (%)	25 (92.6%)	22 (91.7%)	1[a]
Non-opioids, n (%)	7 (28%)	8 (36.4%)	0.23[a]
Opioids, n (%)	2 (8%)	5 (22.7%)	
Mixed, n (%)	16 (64%)	9 (40.9%)	
Antibiotic use, n (%)	20 (74.1%)	5 (20.8%)	0.0001[a]
Nutrition starting time			
Early <48 h	5 (18.5%)	16 (66.7%)	0.0001[a]
Early <72 h	5 (18.5%)	6 (25%)	
Late >72 h	17 (63%)	2 (8.3%)	
Administration route			
Oral, n (%)	24 (88.9%)	23 (95.8%)	0.61[a]
Enteral, n (%)	3 (11.1%)	1 (4.2%)	
Type of diet [c]			
Normal	3 (11.1%)	5 (20.8%)	0.61[a]
Liquid	24 (88.9%)	15 (62.5%)	
Low-fat	0	4 (16.7%)	
Parenteral nutrition use	9 (33.3%)	1 (4.2%)	0.01[b]

PLOS: prolonged length of stay.
[a] Chi-square test.
[b] Fisher's exact test.
[c] Normal: normal for age; liquid: clear liquids; low-fat: fruits and/or vegetables or powdered skim milk.

Table 4 Univariate analysis for the association with the development of prolonged hospital stay (≥7 days).

	OR	95% CI	p
Age	0.91	0.79–1.04	0.16
Recurrence (2 or more events)	0.24	0.07–0.85	0.03
Mild-to-moderate pancreatitis	1	0.99–1.11	0.99
Idiopathic etiology	2	0.44–9.07	0.34
Anatomic/obstructive etiology	0.27	0.08–0.88	0.03
Presence of comorbidities	0.21	0.05–87	0.03
Presence of complications	0.98	0.59–1.63	0.95
Fluid resuscitation	1.25	0.99–1.30	0.67
Early nutrition started	0.05	0.01–0.28	0.001
Antibiotic use	10.86	2.94–40.16	0.001
PN use	11.5	1.33–99.34	0.03
Creatinine mg/dl	4.76	0.54–41.94	0.16
BUN mg/dl	1.1	0.99–1.22	0.07
Total bilirubin mg/dl	8.24	1.55–43.64	*0.01*
AST U/l	1.001	0.99–1.02	0.12
ALT U/l	1.01	1.00–1.02	*0.05*
Albumin mg/dl	0.13	0.03–0.51	*0.003*
Hb g/dl	0.79	0.61—1.04	0.09
Leukocytes $10^3/\mu l$	0.94	0.86—1.02	0.14
Platelets $10^3/\mu l$	0.99	0.98–1.00	*0.05*
Calcium mg/dl	0.44	0.16–1.16	0.09
LDH U/l	1.01	1.00–1.01	*0.03*

OR: odds ratio; 95% CI: 95% confidence interval; p: <0.20.
ALT: alanine aminotransferase; AST: aspartate aminotransferase; BUN: blood urea nitrogen; Hb: hemoglobin; LDH: lactate dehydrogenase; PN: parenteral nutrition.

Table 5 Multivariate analysis for the association with the development of prolonged hospital stay (≥7 days).

	OR	p
Age	2.79	0.09
Recurrence (2 or more events)	1.59	0.21
Anatomic/obstructive etiology	0.62	0.43
Presence of comorbidities	0.99	0.32
Antibiotic use	31.71	*0.006*
Early nutrition started	0.05	*0.02*
PN use	0.11	0.74
Creatinine mg/dl	1.43	0.23
BUN mg/dl	1.01	0.31
Total bilirubin mg/dl	2.74	0.09
AST U/l	0.49	0.48
ALT U/l	0.64	0.42
Albumin mg/dl	1.19	0.27
Hb g/dl	0.37	0.54
Leukocytes $10^3/\mu l$	0.01	0.94
Platelets $10^3/\mu l$	1.56	0.21
Calcium mg/dl	0.03	0.86
LDH U/l	0.79	0.37

OR: odds ratio; 95% CI: 95% confidence interval; area under the curve: 0.86, 95% CI: 0.76–0.96 p: 0.001; Hosmer–Lemeshow test p: 0.87.
ALT: alanine aminotransferase; AST: aspartate aminotransferase; BUN: blood urea nitrogen; Hb: hemoglobin; LDH: lactate dehydrogenase; PN: parenteral nutrition.

(19.6%), corresponding to one mild AP event, 6 moderately severe events, and 3 severe events. The indication for PN was attributed to prolonged fasting, pancreatic-cutaneous fistula, and severe AP, and was combined with oral or enteral feeding.

By subgrouping the study population according to hospital LOS, Table 1 summarizes the demographic and clinical characteristics, in which there were statistically significant differences in relation to age, recurrence (two or more events), grade, etiology, comorbidities, and complications. Likewise, there were significant differences between groups regarding biochemical values at the time of admission, with respect to levels of creatinine, BUN, TB, AST, ALT, albumin, Hb, Hct, platelets, and calcium (Table 2). Table 3 describes the treatment per LOS, in which hospital treatment was heterogeneous for fluid resuscitation, antibiotic use, and time to oral/enteral refeeding.

Table 4 shows the univariate analysis of the variables and their association with PLOS. The variables associated with PLOS underwent a multivariate analysis, in which antibiotic use was significantly associated with a greater risk for PLOS (OR 31.71; 95% CI 2.71–370.65; p = 0.006); likewise, EF (within the first 72 h of admission) was associated with a decrease in the days of hospital LOS (OR 0.05; 95% CI 0.004–0.63; p = 0.02) (Table 5).

Discussion and conclusion

The etiology of AP is varied and involves regional changes that depend on the type of population that is treated at each hospital. In our study, there was a high number of events of anatomic/obstructive etiology, at over 50% (n = 30/51), and when itemized, those with an obstructive cause were the most frequent, contrasting with other national and international studies. In a study conducted at a pediatric referral hospital in Mexico, only 20% of the AP etiologies were obstructive and the most frequent cause was idiopathic, at 34%[3]. Our results also differ importantly from a previous study carried out at our institution, in which more than 50% of the cases of AP were attributable to the use of chemotherapeutic agents[4]. Nevertheless, it is important to remember that the present study did not consider patients that developed AP during their hospitalization due to other diagnoses, which we believe contributed to our finding a different etiology as most frequent. In addition, there was recurrence in 68.2% of our cases.

A multicenter review that evaluated the factors associated with days of hospital LOS, in 7693 discharges of 5507 unique patients (12 years of age, IQR 8–15 years; female sex 55%, n = 4230), concluded that the presence of chronic illnesses (oncologic, gastrointestinal, neurologic, hematologic), PN, and Hispanic ethnicity were factors independently associated with LOS in AP[6]. Likewise, reports described in the literature, focused on the development of predictive models of severity, have enumerated factors associated with the increase in days of hospital LOS[7,8,13–15]. One study found that the presence of pseudocyst or pancreatic necrosis, malnutrition, male sex, and disease severity had an influence on prolonging LOS[7]. Grover et al.[15] identified the presence of two or more SIRS criteria (OR 7.99; p = 0.045) and the requirement of intensive care at admission (OR 12.06; p = 0.027) as independent predictors for longer LOS. In our work, we identified TB (p = 0.01), ALT (p = 0.05), albumin (p = 0.003), platelets (p = 0.05), and LDH (p = 0.03) as factors for PLOS. However, when those variables were evaluated in the multivariate analysis, they were not statistically significant, similar to the results of the above-mentioned studies, in which no associated biomarker could be identified. Another factor associated with PLOS was the presence of severe AP (p = 0.05). That association was previously established by the Cincinnati group[13], utilizing the same methodology as ours to classify AP severity, and documented a higher median LOS (6.1 days; IQR 2.9–14.5 days) in patients with severe AP, compared with the mild AP subgroup (3.9, IQR 2.6–6.4 days; p = 0.0497).

Taking the above into account, one report described a median LOS of 4 days (IQR 3–7 days)[6] and another documented a median of 5 days (IQR 3–10 days)[16]. Both reports contrasted with our findings that were conditioned by the inappropriate trend in the use of antibiotics in practically half of the patients, in which only 60% were regimens authorized by the infectious diseases service. Even though there is no protocol for starting antibiotics, generally they are frequently utilized (31%–82%), up to 90% are started within the first three days, and up to 3 different regimens can be prescribed[17,18]. Neither the NASPGHAN nor the American College of Gastroenterology recommends the prophylactic use of antibiotics, even in severe AP or the presence of necrosis (given that the majority of cases are not infected); they are only recommended in cases of infected necrosis[9,17], and there were no such cases in our study.

Importantly, only 11 of our patients (21.5%), all corresponding to the PLOS group, received aggressive fluid resuscitation upon hospital admission. Aggressive fluid

resuscitation is the cornerstone in the treatment of AP, to prevent potential complications, such as necrosis and organ failure, due to an alteration in the pancreatic microcirculation secondary to events that include hypovolemia, increased capillary permeability, and the formation of microthrombi. Current recommendations state that crystalloids should be started, according to hydration status and hemodynamic status, and with a fluid bolus of 10–20 ml/kg, when there are signs of hemodynamic compromise[9]. Both saline solution (SS) and RL have been evaluated. One study on adults showed that RL, compared with SS, significantly reduced the incidence of SIRS and the development of post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis, but another study found no differences in relation to mortality and LOS duration[19]. Likewise, early EN in combination with aggressive fluid resuscitation (fluid >1.5–2 times requirements in the first 24 h) has been shown to reduce the days of hospital LOS and the presence of severe disease, and no association with pulmonary complications or incidence of re-admission[20]. In that respect, in adults, EN has been shown to be an integral part of treatment and has been associated with a lower incidence of infection, mortality, multiple organ failure, fewer days of hospital LOS, and a decrease in associated complications. Consequently, the intestine plays an important role as an immunologic barrier and EN facilitates that barrier function, preserving the microbiota, preventing bacterial translocation, and lowering the systemic inflammatory response[20,21]. With respect to nutritional treatment, in cases of mild AP, except in the presence of direct contraindications (ileus, fistula, or abdominal compartment syndrome), the ESPGHAN and NASPGHAN recommend that EN be started, combined with a normal oral diet, as soon as possible; ideally within the first 48–72 h of admission. Specialized formulas (elemental, semi-elemental, polymeric) are not necessary, nor is the use of immunoenhanced nutrients[9,10]. Starting EN within the first 48 h in pediatric patients has been shown to be a safe and effective strategy that reduces the days of hospital LOS, the incidence of severe AP, and the need for admission to the intensive care unit. Likewise, in patients with severe AP, it should be attempted within the first 72 h, once hemodynamic stability has been achieved[9,10]. However, in our study, nutrition was begun within that time span in only one patient categorized as having severe AP. In the study by Szabo et al.[22] on 201 children, EN was started within the first 48 h of admission in 75% of the patients, resulting in a statistically significant difference in the days of hospital LOS in that subgroup, compared with the children that remained fasting (2.9 vs 4.9 days, $p < 0.0001$).

Nutritional treatment indication in our institution is different between the hospitalization services, resulting in heterogeneous established managements. Even though fat content has been reported to not increase days of hospital LOS, pain severity, or lipase levels[10,23], the tradition of indicating fasting or a low-fat diet persists, under the concept that ''resting the gut'' prevents stimulating the pancreas, and thus permits faster healing. Evidence justifies the use of EN over PN, for its safety profile, low cost, and lower risk of infection. Likewise, NP is reserved for severe events, for cases in which oral nutrition or EN (nasogastric or nasojejunal) is not tolerated, when it is not possible to begin oral feeding or EN within a 5–7-day period, or administer it in combination with EN, when caloric requirements are not met[9,10,24].

There was one death secondary to septic shock at day 8 of hospitalization, corresponding to a female patient, 12 years and 2 months of age, that was transferred after having spent two weeks in a secondary care hospital. Death due to AP is rare, with a mortality rate that varies from 0% to 21%, as a result of multiple organ failure[25,26].

Our data reaffirm findings from a recent mini meta-analysis, in which the early start of EN significantly reduced days of hospital LOS, compared with *nil per os* (SD = 0.806, $p = 0.034$), and was the only treatment modality showing a clear benefit in improving results in pediatric patients with AP[20]. Despite the current international guidelines that attempt to provide a consensus on the recommendations for treating AP in children[27], there is still a discrepancy among established treatments, especially in nutritional management. With that in mind, it is worth mentioning that our subgroup with PLOS inversely presented with less recurrence and fewer comorbidities and complications, possibly resulting from the heterogeneity in the decision-making for managing AP. Multidisciplinary coordination in the hospitalization treatment of AP would very likely benefit those patients.

The limitations of our case series include its small sample size and retrospective study design.

In conclusion, our study results showed that early nutrition was associated with shorter hospital LOS and that the use of antibiotics was associated with longer hospital stay.

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Conflict of interest

The authors declare that there is no conflict of interest.

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