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CLINICAL AND EPIDEMIOLOGICAL CHARACTERISTICS OF ACUTE PANCREATITIS IN HIGH ALTITUDE RESIDENTS

CARACTERÍSTICAS CLÍNICAS Y EPIDEMIOLÓGICAS DE LA PANCREATITIS AGUDA DE LOS RESIDENTES DE ALTITUD

Geraldine Espinoza-Mayhua [1,a], Amilcar Tinoco-Solórzano [2,b]

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ABSTRACT

Introduction: Acute pancreatitis (AP) may have particular characteristics at high altitude that can affect its severity. **Objective:** To describe the clinical and epidemiological characteristics of AP in residents at high altitude. **Methods:** Observational and descriptive study conducted in a hospital at 3,250 meters above sea level (masl) in Huancayo, Peru. A total of 129 patients with AP between 2017 and 2021 were included. Clinical, demographic, and management characteristics were analyzed. Data were collected at admission and followed until hospital discharge. Statistical analysis was performed using SPSS version 32, describing qualitative variables with frequencies/percentages and quantitative variables with mean/standard deviation or median/interquartile ranges according to the distribution. **Results:** The mean age was 45.8 years; 61.2% were women. The mean BMI was 26.1 kg/m^2, and the hospital stay was 11.1 days. The main cause of AP was biliary (78.3%). The mean SaO2 was 91.6%; PaO2, 68.7 mmHg; PaCO2, 29.4 mmHg; HCO3, 18.8 mEq/L; hemoglobin, 15.5 g; hematocrit, 46.3%; AST, 286.4 U/L; and ALT, 313.9 U/L. The incidence of AP was 38.4 cases per 10,000 admissions. 13.2% were admitted to the ICU, with a mortality rate of 52.9%. The most frequent complications were peri-pancreatic collections (14.7%) and pancreatic necrosis (9.3%). The overall mortality was 13.9%. **Conclusion:** AP at high altitude shows many similar characteristics to sea level; however, differences in SaO2, PaO2, PaCO2, HCO3, and mortality may suggest an influence of hypobaric hypoxia that should be corroborated in further studies.

Keywords: Pancreatitis; Epidemiology; Altitude; Retrospective Studies. (Source: MESH-NLM)

RESUMEN

Introducción: La pancreatitis aguda (PA) podría tener características particulares en altitud que pueden afectar su severidad. **Objetivo:** Describir características clínicas y epidemiológicas de la PA en residentes de altitud. **Métodos:** Estudio observacional y descriptivo realizado en un hospital a 3 250 metros sobre el nivel del mar (msnm) en Huancayo, Perú. Se incluyeron 129 pacientes con PA entre 2017 y 2021. Se analizaron características clínicas, demográficas y de manejo. Los datos se recolectaron al ingreso y se siguieron hasta el alta hospitalaria. El análisis estadístico se realizó usando SPSS versión 32, describiendo variables cualitativas con frecuencias/porcentajes y cuantitativas con media/desviación estándar o mediana/rangos intercuartílicos según la distribución. **Resultados:** La edad media fue 45,8 años; el 61,2% fueron mujeres. El IMC medio fue de 26,1 kg/m^2 y la estancia hospitalaria de 11,1 días. La causa principal de PA fue biliar (78,3%). La media de SaO2 fue 91,6%; de PaO2, 68,7 mmHg; de PaCO2, 29,4 mmHg; de HCO3, 18,8 mEq/L; de hemoglobina, 15,5g; de hematocrito, 46,3%; de TGO, 286,4 U/L y de TGP, 313,9 U/L. La incidencia de PA fue 38,4 casos por cada 10000 ingresos. El 13,2% ingresó a UCI, con una mortalidad del 52,9%. Las complicaciones más frecuentes fueron colecciones peri-pancreáticas (14,7%) y necrosis pancreática (9,3%). La mortalidad global fue 13,9%. **Conclusión:** La PA en altitud muestra muchas características similares al nivel del mar; empero, las diferencias en SaO2, PaO2, PaCO2, HCO3 y la mortalidad, podría sugerir una influencia de la hipoxia hipobárica que deberá ser corroborada en otros estudios.

Palabras clave: Pancreatitis; Epidemiología; Altitud; Estudios Retrospectivos. (Fuente: DeCS- BIREME)

[1] Faculty of Human Medicine, Universidad Peruana Los Andes, Huancayo, Peru.
[2] Department of Intensive and Intermediate Care, Hospital Nacional Ramiro Prialé Prialé, Social Health Insurance of Peru (EsSalud), Huancayo, Peru.
[a] MD, Surgeon.
[b] MD, Specialist in Human Medicine.

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INTRODUCTION

Acute pancreatitis (AP) is an inflammation of the pancreas that can become systemic. The diagnosis of AP is established using at least two of the following criteria: upper abdominal pain radiating to the back, amylase and/or lipase levels three times higher than normal, and typical findings on imaging [1]. The mortality rate of AP varies between one and four percent, with the main causes being biliary (64%) and alcoholic (9%)[1-4].

Over the last twenty years, the incidence of AP has increased by three percent annually, ranging from 0.3 per ten thousand inhabitants in Asia to 13.6 in North America. The average age of the patients is 40.14 years, and the disease affects more females. The most common clinical presentation is abdominal pain, and the length of hospital stay varies between four and six days[4,5]. The geographic environment can influence the presentation of AP. A population is considered at altitude when it is above 1,500 meters above sea level (masl), and a permanent resident is someone who has lived at altitude for at least one year[6]. At altitudes below 3,000 masl, the clinical and epidemiological characteristics of AP are similar to those observed in other parts of the world[7].

However, at altitudes above 3,000 masl, mortality is higher, and AP presents unique challenges due to the overestimation of severity caused by the reduction in arterial oxygen partial pressure (PaO2). This affects the classification of severity in various systems, negatively impacting clinical management [8,9]. Moreover, these studies have limitations in describing demographic, laboratory, imaging, and complications data, and may differ from the sociocultural and epidemiological environment of this study, which could influence the presentation and severity of AP[3,10,11]. Our study seeks to fill the knowledge gap identified by previous studies, addressing the limitations in describing demographic, laboratory, imaging, and complications data. Furthermore, we aim to demonstrate that physiological adaptations caused by life at altitude influence the characteristics of AP, affecting both its presentation and severity in this particular environment [6]. The general objective of this study is to describe the clinical and epidemiological characteristics of AP in residents at altitude.

The specific objectives include determining the incidence, mortality, admission to intensive care units (ICU), and local complications of AP. Our results will allow for improved assessment in the initial diagnosis of AP at altitude.

METHODS

Design and study area

This is an epidemiological, observational, descriptive, longitudinal, and retrospective study. The STROBE checklist for observational studies was used. The study was conducted at a level III-1 hospital located at 3,250 masl, with a barometric pressure of 535 mmHg in Huancayo, Peru. Data were collected at patient admission to the hospital and followed until hospital discharge to determine admission to the operating room, ICU, and mortality.

Population and sample

The population consisted of 129 hospitalized patients from January 2017 to December 2021 at Hospital Regional Daniel Alcides Carrión. No sampling was performed as the entire available population was used. Adult patients who were permanent residents at altitude with AP were included. Patients with incomplete medical records, those referred to other institutions, and those who requested voluntary discharge were excluded.

Variables and instruments

The variables studied included clinical and demographic characteristics. Clinical characteristics comprised vital functions, complete blood count, biochemical tests, arterial gases, abdominal ultrasound, chest X-ray, and abdominal tomography. Demographic variables included age, sex, weight, height, body mass index (BMI), residence at altitude, marital status, education level, occupation, length of hospitalization, signs and symptoms, etiology, and type of management. These were collected using a data collection form, and the technique was the documentation of medical records.

Procedures

Data were collected at patient admission to the hospital and followed until hospital discharge to record events such as admission to the operating room, ICU, and mortality. Patients were clinically evaluated, and corresponding laboratory and imaging tests were

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performed.

Statistical analysis

For statistical processing, SPSS software version 32 was used. In the univariate analysis, the normality of the variables was verified using the Shapiro-Wilk test ($p>0.05$ normal; $p<0.05$ not normal). Qualitative variables were described with frequencies and percentages, quantitative variables with normal distribution with mean and standard deviation, and quantitative variables without normal distribution with median and interquartile ranges.

Ethical considerations

This study obtained its data by reviewing the medical records of adult patients, so it was not necessary to request informed consent. However, the confidentiality of the names of the participants was maintained by recording these data in coded form. Permission was obtained from the hospital to access the data. The study complies with current bioethical research standards and was approved by the Ethics Committee of the Faculty of Human Medicine of the Universidad Peruana Los Andes, Huancayo, Peru.

RESULTS

Data from 129 patients with acute pancreatitis (AP) were analyzed, who were admitted and followed until their hospital discharge. The mean age was 45.8 years, with a predominance of female patients (61.2%). The average BMI was 26.1 kg/m^2, and the mean hospital stay was 11.1 days. The most frequent symptoms were abdominal pain, nausea, and vomiting. The main cause of AP was biliary, and medical management predominated (Table 1).

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Table 1. Epidemiological characteristics of acute pancreatitis in residents of high altitudes.

	Frequency (n)	Percentage (%)	Shapiro Wilk (p-value)
Age (years)	45.8 *	18.7 †	0.944
Sex			
Male	50	38.8	
Female	79	61.2	
Weight (kg)	64.3 *	11.2 †	0.987
Height (m)	1.6 *	0.1 †	0.988
Body Mass Index (kg/m2)	26.1 *	3.6 †	0.990
Residence at high altitude (years)	41.7 *	21.7 †	0.977
Marital status			
Sigle	37	28.7	
Married	33	25.6	
Cohabiting	49	37.9	
Widowed	9	6.9	
Divorced	1	0.8	
Education level			
Illiterate	10	7.8	
Primary	29	22.5	
Secondary	62	48.1	
Higher	28	21.7	

Occupation			
Housewife	60	46.5	
Dependent	54	41.9	
Student	6	4.7	
None	9	6.9	
Hospitalization time (days)	11.1 *	8.2 †	0.856
Signs and Symptoms			
Abdominal pain	129	100	
Nausea	110	85.3	
Vomiting	96	74.4	
Anorexia	19	14.7	
Jaundice	17	13.2	
Fever sensation	12	9.3	
Others	14	10.9	
Etiology			
Biliary	101	78.3	
Idiopathic	23	17.8	
Alcoholic	4	3.1	
Traumatic	1	0.8	
Management			
Medical	77	59.7	
Surgical	52	40.3	

n = 129. * mean. † standard deviation

The values found for clinical parameters were: mean arterial pressure (MAP) of 81.6 mmHg, oxygen saturation (SaO2) of 91.6%, PaO2 of 68.7 mmHg, PaCO2 of 29.4 mmHg, bicarbonate (HCO3) of 18.82 mEq/L, hematocrit of 46.3%, aspartate aminotransferase (AST) of 286.4 U/L, and alanine aminotransferase (ALT) of 313.9 U/L. Chest X-rays were performed on 31 patients (24%), finding pleural effusion in 90.3% of them. Abdominal ultrasound was performed on 124 patients (96.1%), finding gallstones in 66.1%. Abdominal CT scans were performed on 46 patients (35.7%), with 47.8% classified as Balthazar E (Table 2).

Table 2. Clinical characteristics of acute pancreatitis in residents of high altitudes.

	Frequency (n)	Percentage (%)	Shapiro Wilk (p-value)
Vital Signs			
Mean arterial pressure (mmHg)	81.6 *	9.2 †	0.941
Heart rate (lpm)	82.2 *	11.1 †	0.937
Respiratory rate (rpm)	20.9 *	2.2 †	0.740
Oxygen saturation (%)	91.6 *	2.8 †	0.847
Urine output (ml/kg/h)	1.0 *	0.4 †	0.970
Glasgow	15 *	1.0 †	
Complete Blood Count			
Hemoglobin (g/L)	15.5 *	2.3 †	0.987
Hematocrit (%)	46.3 *	7.0 †	0.983
Leukocytes (x109/L)	13.5 *	8.5 †	0.512
Platelets (x109/L)	270.3 *	104.1 †	0.934
Biochemical			
Glucose (mg/dL)	128.7 *	151.7 †	0.277
Urea (mg/dL)	45.7 *	76.1 †	0.280
Creatinine (mg/dL)	1.2 *	1.1 †	0.494
Amylase (U/L)	1841.9 *	3301.9 †	0.359
Lipase (u U/L)	830.7 *	932.0 †	0.776
AST (U/L)	286.4 *	22782.4 †	0.068
ALT (U/L)	313.9 *	48313.4 †	0.066
Bilirubin (mg/dL)	5.2 *	13.0 †	0.247
Alkaline Phosphatase (U/L)	576.6 *	816.8 †	0.459
Arterial Blood Gases			
PH	7.4 *	0.1 †	0.924
PaO2 (mmHg)	68.7 *	14.7 †	0.991
PaCO2 (mmHg)	29.4 *	6.9 †	0.987
HCO3 (mEq/L)	18.8 *	4.3 †	0.972
Base excess (mmol/L)	-5.6 *	6.1 †	0.921
Abdominal Ultrasound			
Not performed	5	3.9	
Performed	124	96.1	
Gallstones	82	66.1	
Choledocholithiasis	33	26.6	
Acute acalculous cholecystopathy	12	9.4	
Excluded gallbladder	6	4.8	
Chest X-ray			
Not performed	98	76	
Performed	31	24	
Pleural effusion	28	90.3	
No pleural effusion	3	9.7	

Abdominal CT Scan		
Not performed	83	64.3
Performed	46	35.7
Balthazar A	1	2.2
Balthazar B	17	37
Balthazar C	3	6.5
Balthazar D	3	6.5
Balthazar E	22	47.8

n = 129. * mean. † standard deviation

27.9% of patients presented local complications, with the most frequent being peripancreatic collections (14.7%) and pancreatic necrosis (9.3%) (Table 3).

Table 3. Local complications of acute pancreatitis in residents of high altitudes.

Complications	Frequency (n)	Percentage (%)
No complications	93	72.1
Peripancreatic collection	19	14.7
Pancreatic necrosis	12	9.3
Pancreatic abscess	2	1.6
Walled-off necrosis	2	1.6
Pancreatic pseudocyst	1	0.8

n = 129

13.2% of patients with acute pancreatitis (AP) were admitted to the ICU. Of these, 47.1% presented pancreatic necrosis, 57.1% were admitted after undergoing surgery, and 47.1% developed septic shock. The mortality rate for patients with AP in the ICU at high altitude was 52.9% (Table 4).

The overall mortality of the 129 patients with acute pancreatitis was 18 patients, representing 13.9%. Of these, 50% had been admitted to the ICU and 27.8% had undergone surgery. The cause of death in 61.1% of cases was septic shock. Abdominal CT scans had not been performed on 55.6% of these patients (Table 5).

Table 4. Characteristics of acute pancreatitis in residents of high altitudes who were admitted to the Intensive Care Unit (ICU).

ICU	Frequency (n)	Percentage (%)
Not admitted	112	86,8
Admitted	17	13,2
Age (years)	53,7	
Sex		
Male	8	47, 2
Female	9	52,9
Admitted to Surgery	8	57.1
Local Complications		
Peripancreatic collection	6	35.3
Pancreatic necrosis	8	47. 1
Pancreatic abscess	1	5.9
Walled-off necrosis	1	5.9
Systemic Complications		
Septic shock	8	47. 1
Acute respiratory failure	3	17.7
Acute renal failure	2	11.8
Mortality	9	52.9

n = 129. ICU: Intensive Care Unit

Table 5. Characteristics of mortality from acute pancreatitis in residents of high altitudes.

	N	%
Total of patients	129	100
Deceased (Mortality)	18	13.9
Age (years)	66,9	
Sex		
Male	7	38.9
Female	11	61.1
Surgical intervention	5	27.8
ICU admission	9	50
No Chest-X-ray performed	11	61.1
No CT scan performed	10	55.6
Local Complications		
Peripancreatic collection	4	22.2
Pancreatic necrosis	4	22.2
Walled-off necrosis	1	5.6
Systemic Complications		
Shock	13	72.2
Respiratory failure	5	27.8
Renal failure	4	22.2

Cause of Death		
Septic shock from abdominal focus	11	61.1
Severe AP	5	27.8
Necro-hemorrhagic AP	1	5.6
Necrotizing AP	1	5.6

n = 129. ICU: Intensive Care Unit. AP: Acute Pancreatitis

DISCUSSION

Globalization has standardized dietary styles, physical activity, weight control, and toxic substance use, leading the high-altitude population to adopt lifestyles similar to those of sea-level residents. In the present study, the predominant age group was adults (36 to 64 years), with a mean age of 45.84 years. The majority of patients were women (61.2%), and 85% were overweight with a BMI over 25 kg/m^2. The average hospital stay was 11.14 days. The most common symptoms were abdominal pain, nausea, and vomiting, with a predominantly biliary etiology, and medical treatment was as frequent as observed at sea level[12,13].

A mean arterial pressure (MAP) of 81.6 mmHg was reported, comparable to patients with AP at sea level. However, it is important to note that healthy residents at altitude have a higher MAP, between 79 and 83 mmHg[14-16]. , likely due to hypobaric hypoxia, suggesting that this elevation is not a consequence of AP but of altitude conditions.

At sea level, AP patients exhibit elevated hemoglobin and hematocrit levels [17]. A hematocrit over 44% increases the risk of developing severe acute pancreatitis and is an independent predictor of mortality. We observed a hematocrit of 46.31%, similar to values reported by Landeo et al. [18]. However, this elevation is common in healthy altitude residents due to the decrease in partial oxygen pressure, which causes tissue hypoxia and an increase in erythropoietin production, raising the red blood cell count [15,19]. Thus, the hematocrit elevation may be more related to altitude than to AP. It remains to be determined whether these values in healthy altitude residents increase the risk of developing severe pancreatitis[3].

The behavior of transaminases in healthy altitude residents is similar to that of sea-level residents, as no alteration in liver cell integrity is observed[20]. In patients with AP at sea level, elevated levels of AST and ALT are reported [11,21]. In the present study, elevated levels of AST (286.4 U/L) and ALT (313.9 U/L) were reported, similar to previous studies conducted at altitude[18].

Abdominal ultrasound was performed in 96.1% of our sample, finding gallstones in 66.1%, results similar to those reported at sea level[21]. CT scans performed at 72 hours from the onset of symptoms are used to determine the severity of AP in patients with unfavorable progression. In the studied population, it was performed in 35.7% of cases, with 47.8% classified as Balthazar E and 37% as Balthazar B, results similar to those observed at sea level[2,18]. However, these results should be analyzed with caution, as CT scans were not performed on the entire sample.

The most frequent complications in patients with AP at altitude were acute peri-pancreatic fluid collections and pancreatic necrosis, which usually resolve spontaneously, results similar to those previously reported[22,23]. 13.2% of patients with AP were admitted to the ICU, a proportion similar to that recorded at sea level[12] 57.1% were admitted after undergoing surgery for pancreatic necrosis, with septic shock being the most frequent reason for admission. The mortality rate in these patients reached 52.9%. Surgical intervention in sterile necrosis is associated with an increase in mortality, whereas infected necrosis should be surgically treated as soon as possible, according to the clinical situation, even before antibiotic therapy [23]. Cholecystectomy is recommended to be performed six weeks after the acute episode[24].

Surgical treatment of sterile AP is associated with mortality [12,13], so evolutionary control through radio-guided abdominal puncture is necessary upon any suspicion of deterioration[25]. Thus, altitude seems not to influence characteristics of AP such as age, sex, BMI, hospital stay, clinical presentation, etiology, MAP, hemoglobin, hematocrit, transaminases, ICU admission, complications, abdominal ultrasound results, and type of management, being similar to those reported at sea level. However, patients with AP at altitude exhibit lower values of SaO2, PaO2, PaCO2, and HCO3, and a higher incidence and mortality than those reported at sea level.

There are evolutionary differences between patients with AP at sea level and those at altitude. However, when comparing patients with AP to the healthy altitude population, no significant differences are observed, which could be explained by the response to chronic hypobaric hypoxia. We reported an SaO2 of 91.6% compared to 96% at sea level in patients with AP [14]. Healthy residents at altitude have an SaO2 between 88% and 97% [15], directly related to the altitude level [16]. Regarding arterial blood gases, the results of this study at altitude show lower values of PaO2, PaCO2, and HCO3 compared to parameters at sea level [26,27]. However, studies in healthy residents at altitude also report decreased values of these parameters, with pH and lactate within normal values [15,28]. Presenting low levels of PaO2, PaCO2, and HCO3 in altitude residents should be considered normal; therefore, in this population, it is better to assess the decrease in pH, the increase in lactate, or the elevation of CRP, which could better predict an evolution to organ dysfunction.

Pleural effusion is an alarming sign indicating an unfavorable progression and allows for the diagnosis of potentially severe AP[22,29]. Its early detection is essential via chest X-ray. It was found that 90.3% of the patients presented pleural effusion, a percentage that doubles other studies [30]. However, only 24% of the sample in this study underwent chest X-ray, so these results must be validated with subsequent studies. The global incidence of AP varies from 0.3 to 13.9 per 10,000 inhabitants [31]. The results of this study show a higher incidence, with 38.44 cases per 10,000 hospital admissions. The global mortality of AP is three to six percent. We observed a mortality rate of 13.9%, much higher than the values at sea level [25]. The higher mortality could be explained by hypobaric hypoxia, which increases the hematocrit [8], although factors related to the surgical management of pancreatic necrosis and evolution to septic shock may also influence. These hypotheses need to be tested. This study aims to be the first step in a new line of research on "Acute Pancreatitis at Altitude," which will continue with subsequent studies.

Among the limitations of our study, we must assume those related to a descriptive study, in which, not having a sea-level control group, we can only propose hypotheses. Another significant bias was the lack of uniformity in imaging studies, which were not performed on the entire sample, potentially leading to information bias. However, despite these limitations, it is one of the few studies analyzing AP at altitude, specifically in a unique environment like the Peruvian highlands, providing valuable data.

CONCLUSIONS

EThe study on AP at altitude showed a mean age of 45.8 years, predominantly women (61.2%), with an average BMI of 26.1 kg/m^2. The average hospital stay was 11.1 days, with common symptoms of abdominal pain, nausea, and vomiting. The main cause was biliary, predominating medical management. The incidence of AP was 38.44 cases per 10,000 hospital admissions, and the mortality rate was 13.9%. 13.2% of patients were admitted to the ICU, with a mortality rate of 52.9%. The most frequent complications were peri-pancreatic collections and pancreatic necrosis. Although, when comparing these results with other studies, altitude does not appear to influence certain clinical and demographic characteristics of AP, lower values of SaO2, PaO2, PaCO2, and HCO3 were observed compared to those reported at sea level, suggesting an impact of hypobaric hypoxia on AP at altitude. We recommend conducting analytical studies comparing altitude populations with sea-level populations to verify if altitude has a direct relationship with the increase in incidence and mortality of AP.

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Correspondence: *Amilcar Tinoco-Solórzano.*
Email: ***amilcartinoco@gmail.com***

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