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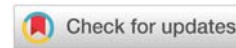
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Retrospective Study

Profile of patients with acute pancreatitis undergoing antibiotic prescription in Brazil

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Abstract

Approximately 5 to 10% of patients with Acute Pancreatitis (AP) develop necrosis and about 30% of these patients develop an infection, more than doubling the risk of mortality. The treatment of AP has undergone a major revolution in recent decades and recent studies advocate minimally invasive procedures and are based on antibiotic therapy. Underuse of antibiotics can lead to inappropriate treatment, while overuse encourages the emergence of resistant bacterial flora. With the objective to evaluate the profile of patients undergoing antibiotic prescription for acute pancreatitis, the authors carried out a retrospective cross-sectional study in a private hospital in Florianópolis, Brazil. Data collection took place through medical records and the variables were analyzed using simple and relative frequency, measures of central tendency, and their respective measures of variability/dispersion and standard deviation. The present study meets the bioethical principles determined by resolution 466/12 of the National Health Council. Of 91 included patients with acute pancreatitis, 38 (41,7%) received antibiotic therapy. Most were female (58,3%), aged between 40 and 59 years (41,7%). Patients that received antibiotics had more frequently severe presentations according to the Atlanta Revised Classification Criteria (47,4%); of those, in 13 (72,2%) the indication occurred in the presence of pancreatic necrosis or collections. A wide range of antibiotics was used, with Meropenem being the most prescribed (39,5%), followed by the combination of Ampicillin with Sulbactam (28,9%). Positive cultures showed carbapenem-resistant *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* in 27,3% of those with positive cultures. The authors conclude that clinical presentation was more severe in cases where there was a need to use antimicrobials. Antibiotics are essential components in the treatment of patients with infection associated with acute pancreatitis and the employment of management protocols that take into account the resistance profile of the local flora is important.

Introduction

Acute Pancreatitis (AP) is characterized by an acute inflammatory process of the pancreas with variable involvement of other tissues or systems [1]. The clinical picture may begin with abdominal pain in the epigastric region, associated with distention with or without nausea and vomiting. In general, the age group between 30 and 60 years is affected [2]. The most frequent etiological factors are gallstones and alcohol consumption in about 80% of cases [3]. The global incidence of AP varies from 4.9 to 73.4 cases per year per 100,000 inhabitants [4]. The incidence in Brazil, according to the Brazilian Institute of Geography and Statistics and the Department of Informatics

of the Unified Health System, varies geographically; the country's average is 19 cases per 100,000 inhabitants [5-7].

AP has 2 critical phases, the early phase covers the first 2 weeks after diagnosis and the late phase starts after the second week. While Systemic Inflammatory Response Syndrome (SIRS) and Organ Failure (OF) dominate the early stage, the late stage is characterized by local complications such as necrosis, pancreatic collections, including infection that is much more prevalent in this stage. Approximately 10% of patients with AP develop pancreatic parenchymal necrosis [8] which is associated with moderate and severe types of the disease [9] and about 30% of these patients develop an infection as



a complication [10]. The risk of mortality more than doubles when pancreatic necrosis is infected [11].

Treatment of infected necrosis includes prescribing broad-spectrum antibiotics, as well as endoscopic, percutaneous, or surgical intervention. In the past, surgical intervention was the first or only option. However, recent studies advocate the “step-up approach”. In this approach, treatment begins with minimally invasive procedures and is based on antibiotic therapy, and surgical intervention is performed only when the initial procedure does not obtain the expected results [9,10].

Analyzing the treatment of infected AP in the last two decades, an extraordinary evolution is observed since the treatment can be started exclusively with antibiotics and only clinical worsening will imply some form of intervention [12]. In this way, antibiotic therapy is considered fundamental for this disease, but excessive use stimulates the emergence of resistant bacterial flora and leads to a reduction of available treatment options, while the underuse of these drugs can lead to inadequate treatment of the infection. In clinical practice, the underlying reasons for prescribing antibiotics in AP are likely to be complex and multifactorial, and the use of antibiotic therapy appropriately, particularly avoiding overprescription, is extremely important for the course of the disease [13]. Thus, the present study seeks a better understanding of the use of antibiotics in the treatment of AP and aims to evaluate the profile of patients undergoing antibiotic prescriptions for AP.

Methods

This is a retrospective cross-sectional study, carried out in the inpatient and emergency units of Baía Sul Hospital, a private hospital in the city of Florianópolis, Santa Catarina – Brazil. Patients diagnosed with AP from January 1, 2011, to July 31, 2019, were studied. Our inclusion criteria were: the diagnosis of AP from at least two of the following: abdominal pain, the elevation of pancreatic enzymes three times the normal value and image signs of AP; age over 18 years, and hospitalization time equal to or greater than three days. Exclusion criteria were unconfirmed diagnosis of AP or insufficient data from medical records.

The variables collected were distributed in (1) demographic characteristics: age (18 to 39/ 40 to 59/ > 60 years) and sex (female/male); (2) clinical characteristics: etiology (biliary/ alcoholic/hypertriglyceridemia/post-ERCP/other), Atlanta Revised Classification (mild/moderate/severe); (3) evolution: length of stay (days), need for Intensive Care Unit (ICU) (yes/no), pancreatic necrosis (yes/no), amount of necrosis (< 30%/ 30–50%/ > 50%), presence of collections pancreatic or peripancreatic (yes/no), surgical intervention (yes/no) and death (yes/no); (4) antibiotic therapy: antibiotic use (yes/no), type of antibiotic, reason for antibiotic prescription (pancreatic necrosis infection / secondary infection of collections / other infectious focus / indication of unknown or unreported origin), duration of use of antibiotic (days), number of antibiotic regimens used in each patient (absolute number), positive culture (bacteria found and sensitivity to antimicrobials).

Data were tabulated in Windows Excel software and imported into the Statistical Package for the Social Science 18.0 Software for statistical analysis. In the descriptive analysis, the qualitative variables were presented in simple and relative frequency, whereas the quantitative variables were analyzed using measures of central tendency (median). Statistical analyzes were performed using Fisher exact test. The significance level adopted was $p < 0,05$.

The present study meets the bioethical principles determined by resolution 466/12 of the National Health Council, through the precepts of beneficence, non-maleficence, justice, equity, and autonomy. Ethical norms that define the use of clinical data for the purpose of scientific studies were adopted. The project was submitted to the UNISUL Ethics Committee and the Project Approval Committee of the Baía-Sul Institute for Teaching and Research and was later approved under CAAE number 17500719.5.0000.5369.

Results

Of the 94 hospitalized patients diagnosed with AP, three were excluded from the analyses due to insufficient data from medical records; 53 (58,3%) did not receive antibiotics and 38 (41,7%) were prescribed antibiotics.

The analysis of the demographic, clinical, and evolution variables of these patients is presented in Table 1. This sample consisted mostly of female patients (58,3%) aged between 40 and 59 years (41,7%). These characteristics did not differ between patients that received or did not receive antibiotics.

Table 1: Analysis of sociodemographic, clinical variables, and evolution of patients undergoing antibiotic therapy in acute pancreatitis, $n = 38$ and patients that did not receive antibiotic therapy in acute pancreatitis $n = 53$.

| | | Antibiotic Therapy | | No Antibiotic | | p - value |
|--------------------------------|------------------------|--------------------|------|---------------|------|-----------|
| | | n | (%) | n | (%) | |
| Gender | Male | 15 | 39,5 | 23 | 43,4 | 0,82 |
| | Female | 23 | 60,5 | 30 | 56,6 | |
| Age | 18 - 39 years | 8 | 21,0 | 21 | 39,7 | 0,07 |
| | 40 - 59 years | 18 | 47,4 | 20 | 37,7 | 0,39 |
| | > 60 years | 12 | 31,6 | 12 | 22,6 | 0,34 |
| Etiology | Biliary | 21 | 55,3 | 10 | 18,9 | 0,0006 |
| | Hypertriglyceridemia | 5 | 13,1 | 11 | 20,7 | 0,41 |
| | Alcoholic | 2 | 5,3 | 2 | 3,8 | 0,12 |
| | Post ERCP | 2 | 5,3 | 1 | 1,9 | 0,56 |
| Atlanta Revised Classification | Other | 8 | 21,0 | 29 | 54,7 | 0,0022 |
| | Mild | 16 | 42,1 | 46 | 86,8 | 0,0001 |
| | Moderate | 4 | 10,5 | 5 | 9,4 | 1,0 |
| | Severe | 18 | 47,4 | 2 | 3,8 | 0,0001 |
| Evolution | CT with necrosis | 8 | 21 | 3 | 5,7 | 0,046 |
| | <30% | 5 | 13,1 | 2 | 3,8 | |
| | 30 - 50% | 1 | 2,6 | 1 | 1,9 | |
| Pancreatic collections | >50% | 2 | 5,3 | 0 | 0 | |
| | Pancreatic collections | 12 | 31,6 | 2 | 3,8 | 0,0006 |
| | ICU | 13 | 34,2 | 1 | 1,9 | 0,0001 |
| | Necrosectomy | 2 | 5,3 | 0 | 0 | 0,17 |
| Death | | 3 | 7,9 | 1 | 1,9 | 0,30 |

n: absolute frequency; %: relative frequency; ERCP: Endoscopic Retrograde Cholangiopancreatography; CT: Computed Tomography; ICU: Intensive Care Unit.



Regarding the clinical characteristics, patients that received antibiotic therapy mostly had pancreatitis of biliary etiology (55.3%), different from the patients that did not receive antibiotics, where the most frequent etiology was another unknown cause (54,7%); with a significant difference (p -value $< 0,05$). The presentation according to the Atlanta Revised Classification Criteria was most frequently severe (47.4%) in patients that received antibiotics and mild (86,8%) in patients that did not receive antibiotics; with a significant difference (p -value $< 0,05$). (Table 1).

As for the evolution of the patients that received antibiotic therapy, eight (21%) had pancreatic tissue necrosis identified on Computed Tomography (CT), among these, 7 had collections associated with necrosis. In addition to these, five other patients had pancreatic or peripancreatic collections alone, thus totaling the presence of pancreatic or peripancreatic collections in twelve (31.6%) patients. Thirteen (34.2%) were required to stay in the Intensive Care Unit (ICU) and only two (5.3%) patients underwent pancreatic surgery – necrosectomy. Among the 2 patients who underwent pancreatic necrosectomy, one died after the procedure. In this series, three patients (7.9%) died, all had severe acute pancreatitis, and the other two died of organ dysfunction resulting from the Systemic Inflammatory Response Syndrome in the initial phase of the disease (Table 1).

The patients that did not receive antibiotic therapy had a disease evolution with less necrosis (5,7%), collections (3,8%), or ICU stay (1,9%), with a significant difference from those that did receive antibiotic therapy (p -value $< 0,05$). However, although the frequency of pancreatic surgery and death are also lower, the difference was not significant (Table 1).

The descriptive analysis regarding the use of antibiotics according to the Atlanta Revised Classification Criteria for pancreatitis is presented in Table 2. Assessed by the severity of the episode, 16 (42.1%) patients who received antibiotic therapy had mild forms of the disease, and 12 (75%) of these patients were indicated for an extrapancreatic infection discovered during a hospital stay. On the other hand, 18 (47.4%) of the patients treated with antibiotics had severe AP and in 13 (72.2%) of these, the indication occurred in the presence of necrosis or pancreatic or peripancreatic collections. Of the total of 38 patients, 7 (18.4%) were prescribed antibiotics without a description of the indication for their use reported in the medical records and 18 (47.3%) used this drug due to extrapancreatic infection, being cholecystitis the most prevalent.

The length of hospital stay was longer in patients with severe AP, with a median of 23 days. Regarding the length of the antibiotic therapy, the median was 15 days in moderate and severe AP (Table 2).

Tables 3 and 4 describe the types of antibiotics used, along with their indication; Meropenem, a broad-spectrum antibiotic, was the most frequently prescribed (15 patients [39.5%]), followed by the combination of Ampicillin with Sulbactam (11 patients [28.9%]). In most cases, the prescription of meropenem was an option when the patient exhibited necrosis or pancreatic or peripancreatic collections

Table 2: Antibiotic use in acute pancreatitis according to the Atlanta Revised Classification Criteria $n = 38$.

| | Mild | Moderate | Severe | Total |
|---|------------|-----------|------------|------------|
| Number of patients | 16 (42,1%) | 4 (10,5%) | 18 (47,4%) | 38 |
| Indication for the use of antibiotics | | | | |
| Not reported | 4 | 1 | 2 | 7 (18,4%) |
| Necrosis and/or collections | 0 | 1 | 12 | 13 (34,2%) |
| Extrapancreatic infections | 12 | 2 | 4 | 18 (47,3%) |
| Colecistitis | 7 | 0 | 1 | 8 |
| Pneumonia | 1 | 1 | 2 | 4 |
| UTI | 2 | 1 | 0 | 3 |
| Colangitis | 1 | 0 | 1 | 2 |
| Other | 1 | 0 | 0 | 1 |
| Hospitalization | | | | |
| Length of antibiotic use – days (median) | 4 | 15 | 15 | 8,5 |
| Length of hospitalization - days (median) | 5 | 16 | 23 | 10,5 |

UTI (Urinary Tract Infection).

Table 3: Frequency of antibiotic use, $n = 38$.

| Antibiotic | n | (%) |
|---|----|------|
| Meropenem | 15 | 39,5 |
| Ampicilina + Sulbactam | 11 | 28,9 |
| Ceftriaxon | 8 | 21,0 |
| Metronidazol | 8 | 21,0 |
| Ciprofloxacin | 7 | 18,4 |
| Piperacilin + Tazobactam | 6 | 15,8 |
| Polimixin B | 3 | 7,9 |
| Vancomicin | 2 | 5,3 |
| Ampicilin | 2 | 5,3 |
| Azitromicin | 1 | 2,6 |
| Levofloxacin | 1 | 2,6 |
| Linezolid | 1 | 2,6 |
| Clindamicin | 1 | 2,6 |
| Ceftazidime | 1 | 2,6 |
| Cefepime | 1 | 2,6 |
| Number of antibiotic regimens per patient | | |
| 1 | 18 | 47,4 |
| 2 | 14 | 36,8 |
| 3 | 2 | 5,3 |
| 4 | 4 | 10,5 |

n: absolute frequency; %: relative frequency.

on imaging. Eighteen patients (47.4%) used only one antibiotic regimen during their hospitalization, while 14 (36.8%) received two different regimens, and the other 6 patients used three or more regimens. The prescription of a greater number of antimicrobial regimens occurred more frequently in patients with the presence of necrosis or pancreatic or peripancreatic collections than in those in which the treatment was prescribed for other indications.



Tables 5-7 illustrate the different pathogens isolated and the antimicrobial susceptibility profile. Among the 38 patients evaluated in this study, 11 (28.9%) had positive cultures, of these, most had pancreatic necrosis or collections identified in CT scans. Two of these pathogens are highlighted as being Gram-negative bacteria capable of multi-resistance to antibiotics, namely: *Klebsiella pneumoniae* (2 patients [18.2%]) and *Pseudomonas aeruginosa* (2 patients [18.2%]). Both bacteria showed resistance to the class of antibiotics Carbapenems (Ertapenem, Meropenem, and Imipenem) and potent penicillins associated with Beta-lactamase inhibitors such as Piperacillin plus Tazobactam. On the other hand, *Escherichia coli*, also a Gram-negative bacterium, showed resistance only to Quinolones (Ciprofloxacin and Norfloxacin) (Table 6).

Discussion

In the population of patients hospitalized for acute pancreatitis, the frequency of antibiotic prescription is similar to that found in the literature and reflects the indication, not only for suspected infection of areas of pancreatic necrosis or collections but also for identified extrapancreatic infections. In the literature review published by Baltatzis, et al. in 2016 [13], there are sometimes even higher percentages of antibiotic prescriptions than in the present study, due to the indication for prophylaxis, which was not identified in this research. The demographic and clinical profile of patients undergoing

Table 4: Antimicrobial prescription according to the indication for antibiotic use.

| | Meropenem | Number of antimicrobial regimens |
|---|------------|----------------------------------|
| Necrosis / collections | 11 (84,6%) | 1 in 46,1% |
| | | 2 in 23,1% |
| | | 3 in 7,7% |
| | | 4 in 23,1% |
| Infection of undefined origin and extrapancreatic infection | 4 (16%) | 1 in 48% |
| | | 2 in 44% |
| | | 3 in 4% |
| | | 4 in 4% |

Table 5: Pathogens found in positive cultures of patients who were prescribed antibiotics, n = 11.

| Patógeno | n | (%) |
|-----------------------------------|---|------|
| Gram-positive | | |
| <i>Enterococcus faecium</i> | 1 | 9 |
| <i>Enterococcus faecalis</i> | 1 | 9 |
| <i>Staphylococcus hominis</i> | 1 | 9 |
| Gram-negative | | |
| <i>Haemophilus parainfluenzae</i> | 1 | 9 |
| <i>Klebsiella pneumoniae</i> | 2 | 18,1 |
| <i>Pseudomonas aeruginosa</i> | 2 | 18,1 |
| <i>Escherichia coli</i> | 4 | 36,3 |

n: absolute frequency; %: relative frequency.

Table 6: Antibiotic resistance of Gram-negative bacteria found in positive cultures.

| Bacteria | Antibiotic resistance |
|-------------------------------|-----------------------|
| <i>Klebsiella pneumoniae</i> | Ampicillin |
| | Imipenem |
| | Ertapenem |
| | Meropenem |
| <i>Pseudomonas aeruginosa</i> | Amicacin |
| | Cefepime |
| | Ceftazedime |
| | Levofloxacin |
| | Ciprofloxacin |
| | Gentamicin |
| | Imipenem |
| | Ertapenem |
| | Meropenem |
| Piperacilin + Tazobactam | |
| <i>Escherichia coli</i> | Ciprofloxacin |
| | Norfloxacin |

Table 7: Description of culture results, antimicrobial resistance profile and collection site according to the indication for antibiotic use.

| | Culture result | Antimicrobial resistance profile | Collection site | |
|---|------------------------------|---|---------------------|------------|
| Necrosis / collection | <i>Escherichia coli</i> | Multi sensitive | Abdominal secretion | |
| | | | Blood | |
| | | Multi sensitive | Blood | |
| | | | No antibiogram | |
| | | Carbapenemics and Beta lactamics with Beta-lactamase inhibitors | Blood | |
| | | | | |
| Carbapenemics and Beta lactamics with Beta-lactamase inhibitors | Blood | | | |
| | | | | |
| Penicillin | Blood | | | |
| | | | | |
| Extrapancreatic infection | <i>Klebsiella Pneumoniae</i> | Ampicillin | Blood | |
| | | | UTI | Urine |
| | | | | Colangitis |
| | | | Other | |
| | | | | |

UTI: Urinary Tract Infection.

antibiotic therapy in the presence of acute pancreatitis analyzed in the present study is in agreement with the literature, since the gender and age group most commonly affected by this disease are female and aged between 40 and 59 years. The higher frequency of biliary etiology, in the group of patients that needed antibiotic therapy, could be explained by the possibility of the presence of an extrapancreatic infection, such

as cholecystitis or cholangitis. The high percentage of severe AP is justified by a sample of infected patients, which causes morbidity and mortality to those affected [5,13,14].

During the clinical course, only two of the patients, included in the present study, with necrosis of the pancreatic parenchyma, evolved with clinical worsening after starting treatment and thus underwent necrosectomy. These findings correlate with the current “step-up approach” since necrosectomy is considered a significant surgical trauma with high rates of morbidity, mortality, and pancreatic insufficiency [12,15].

The PANTER Trial, a multicenter and randomized study, compared treatment by open necrosectomy with the “Step up approach”, which consists of a staged therapy and has percutaneous drainage as the first invasive intervention. From this work, the concept of a minimally invasive approach was disseminated, reserving necrosectomy for cases of therapeutic failure [16]. Other studies corroborate this new way of intervening in the treatment of AP, Runzi, et al. [17] published the first large series of conservative treatments for infected pancreatic necrosis, evaluating 28 patients, of whom 16 did not undergo surgery, among these, 6 patients evolved satisfactorily and the mortality presented in the study was 12.5%. Russian, et al. [12] presented a series of 6 patients with necrosis and pancreatic infection evidenced by gas in the retroperitoneum, treated exclusively with antibiotics, resulting in a favorable outcome. Thus, based on the literature, it is evident that the beginning of treatment should be exclusive to antibiotics, being restricted to cases with previously diagnosed infection, a situation that, in general, occurs from the second or third week of AP evolution. The antibiotics most frequently used in cases of pancreatic necrosis infection are those with good penetration into the pancreatic tissue, such as carbapenems, quinolones, and metronidazole.

In the present research, the indication for the use of antibiotics was clear in most cases, but in 18.4% of the patients, it was not possible to identify the indication of the prescribed antibiotic therapy. This data may reflect the limitation inherent to the retrospective study that depends on the proper completion of the medical record, but it may also indicate that might have happened an unjustified antibiotic prescription, that is, without clinical, laboratory, or imaging evidence of an infection. I also happened in some countries such as Canada (25.5%) [18] and the United Kingdom (30.7%) [13] where patients with AP received antibiotics unjustifiably. In these cases, the possibility of antibiotic prophylaxis is highlighted. According to the IPA/APA guidelines, the use of antibiotic prophylaxis for the prevention of infectious complications in AP is not recommended. According to a recent meta-analysis of 14 randomized clinical trials, there is no evidence to support the routine use of this practice [19]. As for prophylaxis in extrapancreatic infections, the study by Mourad, et al. [20] showed no improvement in the results, demonstrating that mortality (9% vs. 0%, $p = 0.043$) and morbidity (36% vs. 5%, $p = 0.002$) of those treated prophylactically were significantly higher compared to those not treated. A potential reason for not

using prophylaxis is the development of multidrug-resistant bacteria, which is associated with prolonged hospital stay and clinical evolution with unfavorable results [21,22].

A factor that interferes in the decision of starting antibiotics in AP is the difficulty in distinguishing between SIRS and infection since clinical signs such as fever, tachycardia and high leukocyte count can be similar in both scenarios [13]. In order to elucidate these two entities, some studies suggest that procalcitonin would be a good marker for suspected infection in the initial phase of AP since its levels rapidly increase in response to a pro-inflammatory stimulus of bacterial origin and fall after success. Of treatment [23,24].

Regarding the use of antibiotics and the severity of AP, most patients with mild disease in the present study that received antibiotics, were treated for an extrapancreatic infection. According to Baltatzis, et al. [13], there is substantial use of antibiotics during the clinical course of AP with a tendency to excess in patients with mild AP. In this scenario, unless there is an indication for the prescription of antibiotics in the treatment of proven infection, there is no benefit to their use. Of the patients with severe AP submitted to antibiotic therapy, most had complications such as necrosis and/or pancreatic and peripancreatic collections. The indications for the prescription of antimicrobials in the population of patients with severe AP are in accordance with critical conditions manifested by infections that carry a high risk of mortality.

According to Brown, et al. [25], approximately one-third of patients with AP suffer complications from an extrapancreatic infection. Jung, et al. [24] state that pneumonia is the most common extra-abdominal infection in patients with severe AP admitted to the ICU and Moka, et al. [14] suggest that pneumonia in patients with AP prolongs the course of hospitalization and increases mortality.

The most used antibiotics in the present study were Meropenem and Ampicillin plus Sulbactam, followed by Ceftriaxone and Metronidazole. The prescription of Meropenem was used in most patients with infection of pancreatic and peripancreatic tissue, based on adequate penetration in these tissues. The number of antibiotic regimens was higher in patients with local complications from AP, reflecting the severity of this group of patients, however, continued surveillance is required as multiple broad spectrum regimens create a high risk of resistant flora in patients who have severe disease [13].

Of the pathogens found, gram-negative bacteria were the most prevalent, which is consistent with the literature, since *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Escherichia coli* are considered the predominant agents in AP patients [14,25]. Gram-negative bacteria are the main microorganisms causing secondary infection in AP, in which nosocomial infections play an important role. The drug resistance profile of these bacteria is seriously threatening and antibiotics commonly used in AP are gradually losing their effectiveness [26].



In this study, both *Klebsiella pneumoniae* and *Pseudomonas aeruginosa* were resistant to the class of Carbapenems (Ertapenem, Meropenem, and Imipenem) and potent penicillins associated with Beta-lactamase inhibitors such as Piperacillin plus Tazobactam. Moka, et al. [14] reported a marked trend of resistance to carbapenems, amoxicillin, and third-generation cephalosporins in patients with AP. In contrast, Su, et al. [27] demonstrated that 100% of the gram-negative bacteria found were sensitive to carbapenems. At the Baía Sul Hospital, where the research was carried out, the percentage of resistance of *Klebsiella pneumoniae* to carbapenems is 25% both in 2018 and 2019, and for beta-lactams with beta-lactamase inhibitor the percentage of resistance reduced from 44 to 36% from 2018 to 2019; the percentage of resistance of *Pseudomonas aeruginosa* to carbapenems is 22% in 2018 and 29% in 2019 and the percentage of resistance to beta-lactams with a beta-lactamase inhibitor is 18% in 2018 and 29% in 2019; in the case of *Escherichia coli*, the percentage of resistance to quinolones is 19% in 2018 and 21% in 2019. Our series identified bacteria with worse sensitivity profiles than in most infections in the same hospital, in the current study, 44,4% of samples with gram-negative bacteria were resistant to these antibiotics. One hypothesis for the high incidence of resistance to carbapenems is given by the severity of these patients, with the need for multiple antimicrobial regimens used in some of them; as well as the need for prolonged ICU stay where the hospital flora is selected due to the use of third and fourth generation antibiotics in most patients admitted [14]. On the other hand, the gram-negative bacterium *Escherichia coli* showed resistance only to Quinolones (Ciprofloxacin and Norfloxacin). This is relevant since the current trend is for a growing phenomenon in antibiotic resistance, resulting in multidrug-resistant *Escherichia coli* [14].

The study has some limitations, such as the retrospective method, which is subject to insufficient data in electronic medical records, the sample has a small number of patients, and the difficulty in determining the reason why a patient received antibiotic therapy since part of the infections documented did not have proof of this in their medical records, possibly in the case of suspected infection. Thus, it appears that the present work opens the opportunity for future studies, ideally prospective, that can expand the investigation on the use of antibiotics in AP, a subject of extreme importance in clinical practice.

Conclusion

Based on the information obtained through the collection of data from patients who were prescribed antibiotics in the presence of acute pancreatitis, we concluded that:

There was adherence to the new minimally invasive approach in the treatment of acute pancreatitis, reserving necrosectomy for cases of therapeutic failure, which determined low mortality.

The demographic profile of patients prescribed antibiotics in acute pancreatitis is similar to that of other patients with the same disease; however, the clinical presentation is more severe in cases where there is a need to use antimicrobials.

Antibiotics are essential in the treatment of patients with infection associated with acute pancreatitis, which makes it relevant to employ management protocols that take into account the resistance profile of the local flora.

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