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Retrospective Cohort Study

Epidemiological trends in acute pancreatitis: A retrospective cohort in a tertiary center over a seven year period

Ghiț ă AI *et al.* Epidemiological trends in AP

Abstract

BACKGROUND

Acute pancreatitis (AP) remains a major cause of hospitalization and mortality with important health-related costs worldwide. Using an electronic database of a large tertiary center, we estimated the incidence, etiology, severity and costs of hospitalized AP cases in southern Romania.

AIM

To estimate the incidence, cost and tobacco usage of hospitalized AP cases in southern Romania and to update and upgrade the knowledge we have on the etiology, severity (in regard to RAC), outcome, morphology and local complications of AP.

METHODS

We performed an electronic health care records search on AP patients treated at University Hospital Bucharest (Spitalul Universitar de Urgență București) between 2015 and 2022. The incidence, etiology, and severity were calculated; potential risk factors were evaluated, and the hospitalization costs of AP were documented and analyzed. The cohort of this study is part of the BUCHarest - Acute Pancreatitis Index registry.

RESULTS

A total of 947 consecutive episodes of AP where the patients were hospitalized in the gastroenterology department were analyzed, with 79.45% as 1st episode and the rest recurrent. The majority of the patients were males (68.9%). Alcoholic (45.7%), idiopathic (16.4%) and biliary (15.2%) were the main causes. The incidence was estimated at 29.2 episodes/100000 people. The median length of stay was 7 d. The median daily cost was 747.96 RON (165 EUR). There was a high prevalence of active tobacco smokers (68.5%). The prevalence of severe disease was 11.1%. The admission rate to the intensive care unit was 4.6%, with a mortality rate of 38.6%. The overall mortality was 5.5%.

CONCLUSION

We estimated the incidence of AP at 29.2 episodes that required hospitalization per 100000 people. The majority of our cases were found in males (68.9%) and were related to alcohol abuse (45.7%). Out of the cases we were able to find data regarding tobacco usage, the majority were active smokers (68.5%). Most patients had a mild course (54.4%), with a mortality rate of 5.5%. Interstitial AP prevailed (45.3%). The median daily cost of hospitalization was 747.96 RON (165 EUR).

Key Words: Acute pancreatitis; Epidemiology; Revised Atlanta Classification; Mortality; Outcome; Cost

Ghiț ă AI, Pahomeanu MR, Negreanu L. Epidemiological trends in acute pancreatitis: A retrospective cohort in a tertiary center over a seven year period. *World J Methodol* 2023; In press

Core Tip: Retrospective cohort study on 947 consecutive hospitalized episodes (in 829 patients) of acute pancreatitis (AP) with the aim of estimating the incidence, cost and tobacco usage in AP cases and to update & upgrade the knowledge we have on the etiology, severity (as stated in Revised Atlanta Classification), outcome, morphology and complications of AP. Out of our study resulted that: the majority of patients were males (68.9%); alcoholic etiology prevailed (45.7%); estimated incidence: 29.2 episodes/100000 people; median daily cost: 165 EUR; median hospitalization 7 d; majority active tobacco smokers (68.5%); 11,1% severe disease; admission to intensive care unit 4.6%; overall mortality 5.5%.

INTRODUCTION

Acute pancreatitis (AP) remains one of the main conditions treated in gastroenterological departments worldwide and is a common cause of hospitalization.

With an incidence of 3.8-74.8 cases per 100000 in Europe^[1]. AP remains a burden for health care system expenditures, although approximately 75%-80% of patients will develop only a mild clinical course^[2]. Positive diagnosis is based on at least 2 positive criteria from the following: Lypasemia (or amylasemia) higher than 3 times the normal range, a clinical presentation (upper abdominal pain that radiates to the back, nausea, vomiting, *etc.*) or imaging criteria (ultrasound, contrast-enhanced computed-tomography, contrast-enhanced magnetic resonance imaging)^[3].

¹ Updated population-based studies on AP in Romania are lacking. Our aim was to evaluate the current data for AP in a tertiary center in Bucharest. The objective of this paper is to estimate the incidence, cost and tobacco usage of hospitalized AP cases in southern Romania and to update and upgrade the knowledge we have on the etiology, severity (in regard to RAC), outcome, morphology and local complications of AP. Although most of those issues have already been addressed in other populations, there is a high degree of heterogeneity in the worldwide and time-related AP demographics, etiologies, management practices, and outcomes^[4]. A previous study conducted in 2005 on a similar population^[5] of patients from a gastroenterological services found a dominance of alcohol-related pancreatitis. However, that study had a relatively small number of patients and could not estimate the incidence and stratify etiologies other than alcoholic, biliary, post-endoscopic retrograde cholangiopancreatography and hypertriglyceridemia.

MATERIALS AND METHODS

Patients

For this observational retrospective study, we inquired about the Spitalul Universitar de Urgență București (Emergency University Hospital of Bucharest) digital database for cases of AP [International Classification of Diseases 10 code: K85, B25.2, B26.3], in which adult patients were admitted to gastroenterological wards between 1 June 2015 and 1 April 2022.

The inquiry obtained 1074 consecutive episodes (Table 1). All of the patients were screened by the authors for miscoding, revealing that all 1074 fulfilled at least 2 criteria for AP (as they are mentioned in the Revised Atlanta Classification)^[6], out of which 126 were chronic pancreatitis, so we excluded them from this study. We collected the following data: Sex, month of admission, age, number of days of admission, number of days of admission to the intensive care unit (ICU) (if it were the case), outcome at discharge, type of severity according to the Atlanta Revised Classification^[6], type of morphology according to the Atlanta Revised Classification, probable etiology, urban-rural residence, county of origin, previous history of pancreatitis, smoking habits and cost of admittance.

Morphology was assessed according to the Atlanta Revised Classification by the authors' consensus from the available imagistic investigation. We took into consideration (arranged by the power of evidence) abdominal ultrasound, endoscopic ultrasound, contrast-enhanced computer tomography, and contrast-enhanced magnetic resonance.

This cohort is represented only by the patients admitted to the gastroenterology department and represents the BUCharest - Acute Pancreatitis Index (BUC-API) 1 - Gastroenterology cohort. For the aforementioned cohort, we took into consideration demographic, clinical, biological and imagistic data obtained from the electronic database of Emergency University Hospital of Bucharest. The population of this cohort is represented by 918 patients, with 1074 episodes of AP, recurrent AP and acute-on-chronic pancreatitis involving patients who were admitted to our department from 1 June 2015 to 1 April 2022 with AP. Details regarding the number of unique patients are from the BUC-API 1 - Gastroenterology cohort can be found in Table 1.

Statistical analysis

The database was organized using Microsoft Excel 2019[®]. For the statistical analysis of the data, we used crosstab analysis, frequency analysis, linear regression, ANOVA, chi-

square test, Fisher exact test, and goodness of fit run on the statistical program IBM SPSS Statistics version 29.0.0.0©.

RESULTS

Estimated incidence of AP

Our hospital serves as a tertiary referral center for a population of approximately 950 thousand inhabitants, and we are admitting half of the AP patients in our hospital as the other half being admitted to surgical wards. Our search identified 1074 episodes, of which 126 were miscoded as AP, being in fact acute-on-chronic pancreatitis. The remaining 947 consecutive episodes were AP to which the patients were admitted to the gastroenterological wards of our hospital in the timespan of 6 years and 10 mo, between 1st of June 2015 and 1st of April 2022. Based on the aforementioned statistics, we managed to estimate an incidence of AP in southern Romania of 29.2 episodes per 100000 people. This incidence means that we estimate approximately 5900 hospitalizations for AP annually at the country level.

Demographics

We found a total of 947 consecutive episodes that fulfilled at least 2 out of the 3 diagnostic criteria and were not chronic pancreatitis. Of them, 75.39% ($n = 714$) of the patients did not have any history of AP, and the others had at least one previous episode of AP but without signs of chronic disease and/or pancreatic malignancy.

In total, 68.88% ($n = 652$) of the cases were in male patients, and the median age was 54 years (± 15.9). By type of residence, 73.1% ($n = 692$) of the patients were from cities, 25.4% ($n = 241$) were from the countryside, and the remaining 1.4% ($n = 14$) did not have a fixed residence within Romania.

Etiology

We have defined the etiology of AP in regard to 16 possible causes and another 18 possible intricate etiologies, based on how they were defined as predisposing

conditions in Sleisenger and Fordtrans - Gastrointestinal and Liver diseases - 10th edition^[7]. We have defined some of the etiologies as follows: (1) Alcohol-related^[8]: Regular alcoholic consumption (obtained through anamnesis) and/or indirect elements in cases without an apparent etiology, such as macrocytosis, icterical cholestasis, DeRitis ratio^[9] > 2 in middle-aged men, Dupuytren contracture, *etc.* We could not quantify the usage of CAGE Questionnaire^[10] from the medical records we reviewed; (2) Biliary: Imagistic findings (ultrasonographic, computer tomography or magnetic-resonance) with elevated aminotransferases (alanine aminotransferase or aspartate aminotransferase)^[8]; (3) Hypertriglyceridemia: Triglycerides > 750 mg/dL, we sought to use a threshold formed from an average between 1000 mg/dL^[8], and the one recommended for treatment of hypertriglyceridemia by ATP III guideline (500 mg/dL)^[11]; (4) Trauma: Anamnesis, a high creatine kinase; and (5) Diabetes mellitus: No apparent etiology and at least one of the following: Hemoglobin A1c > 7.5% or glycemia > 250 mg/dL at two consecutive findings (without prior history of diabetes mellitus).

All other single etiologies were classified by the authors' consensus. We found 45.7% ($n = 433$) of the cases to be related to alcohol consumption and 15.2% ($n = 144$) were related to gallstones. Among other remarkable etiologies, we found 16.4% ($n = 155$) idiopathic, 3.5% ($n = 33$) hypertriglyceridemia-related, 3% ($n = 28$) diabetes mellitus-related, and 2.5% ($n = 25$) pharmacological (Table 2).

Tobacco usage

We were able to identify tobacco usage in 40.5% of the patients ($n = 384$), out of which 68.5% ($n = 263$) were active smokers and another 22.4% ($n = 86$) ceased smoking tobacco more than 4 wk prior to hospitalization. We could not objectively quantify the number of pack-years from the medical records.

Severity and outcome

At discharge, we found that 54.4% ($n = 515$) had mild AP, 34.5% ($n = 327$) had a moderately severe course of disease, and the latter 11.1% ($n = 105$) had severe disease. A total of 4.6% ($n = 44$) were admitted to the ICU, with a mortality rate of 38.6% ($n = 17$) and a median length of stay within the ICU of 4 d (± 0.8). Regarding the entire population, the mortality rate observed was 5.5% ($n = 52$), with a healing rate of 83.2% ($n = 788$). The outcome is presented in detail in Table 3.

Regarding morphology, we retrieved information from the medical records in 73.4% of the patients. The most frequently encountered morphology was 45.3% ($n = 429$) who had interstitial edema, followed by 11.3% ($n = 107$) with a normal pancreas and 7.4% ($n = 70$) with acute peripancreatic collections. Necrosis as understood by acute necrotic collection and walled-off necrosis was encountered in 3.9% ($n = 37$) of the patients. Table 4 shows the available details about the morphology.

Hospitalization and estimated costs

The length of hospitalization varied greatly, with a median of 7 d (± 6.05) and a maximum of 101 d. Regarding the month of hospitalization, most of the patients were hospitalized in May (11.4%, $n = 108$), and the fewest were hospitalized in February ($n = 62$). All the cases by month of hospitalization are shown in Figure 1. The median total cost was 5177.5 RON (± 6238.89) (approximately 1100 EUR), with a maximum of 100762 RON (approximately 22400 EUR). The median daily cost, was calculated to be 747.96 RON (± 411) (approximately 165 EUR). Considering the data, we were able to calculate the cost of hospitalization of the entire population included in this study at 4958226.84 RON (approximately 1 million EUR) and to estimate the annual cost of hospitalization for this disease in Romania at 30890748 RON (approximately 6.3 million EUR).

DISCUSSION

Previous reports estimated that the incidence of AP varied across Europe between 4.6 and 100 cases/100000 people annually^[1,2,5,12]. We have estimated an incidence of 29.2 cases/100000 people, or approximately 5900 episodes annually throughout the entire

country, which is an expected and moderate profile of incidence. We could not find any specific data about incidence in our country, so this is most likely the first attempt to estimate the incidence of AP in Romania.

To the best of our knowledge, this is the first attempt to estimate the cost of hospitalization in Romania. We observed a median total cost of 5177.5 RON (approximately 1100 EUR) and a median daily cost of 747.96 RON (approximately 165 EUR). Comparing it to other studies^[12,13], we found a median daily cost similar to that in Spain (143 EUR) but far lower than the median total cost of 10069 USD in the United States in 2010. A possible limitation resides in the fact that all our patients were hospitalized in public-owned facilities, so it is possible that some of the costs were underestimated.

Smoking might be an independent risk factor for AP severity and evolution^[14-16]. In our study, we were able to find that more than two-thirds of the patients smoked actively, while another 22.4% were former smokers. These data show us a higher percentage of active smokers in the AP population than those reported in the general population of Romania (68.5% *vs* 30%, as stated by the 2021 Eurobarometer). We will soon try to observe if there is any correlation between smoking tobacco products and AP in another paper.

The median length of stay in AP varies in the literature from 4 d in Finland^[17] to 9 d in Chile^[18] and 10 d in Spain^[12]. We found a length of stay of 7 d, which is similar to other previously published studies. Regarding the seasonality of AP, we found a peak in incidence in May, which is somewhat similar to the findings from a Chinese study and might be related to cultural habits^[19].

Previous papers found a high prevalence of alcohol-related AP with a gallstone-to-alcohol ratio of 0.39 in 2005 in Romania^[2,5], similar in trend to other Eastern and Northern European countries^[17,20]. In India, the gallstone-to-alcohol ratio seems to be very close to 1 (0.95), with other etiologies being negligible^[21]. In Spain and the Americas^[12,18,22], the gallstone etiology seems to prevail, while in China^[23], although the gallstone cause prevails, hypertriglyceridemia appears to be a highly important cause

(probably due to lower rates of alcoholism in that region). Globally, it seems that gallstone-related AP is the most common^[24]. In our cohort of patients, alcoholic etiology was most prevalent (45.7%), with a lower than previously reported gallstone-to-alcohol ratio of 0.33 and an overall relative lower rate of all the main four etiologies (alcohol, biliary, idiopathic and hypertriglyceridemia).

In regard to the outcomes, we observed lower rates of mild AP than those of other studies that have stratified severity in regard to the Revised Atlanta Classification^[18,25]. We observed a lower (4 *vs* 8 d) median length of stay in the ICU than those observed in China^[26] or Australia^[27] but higher mortality rates than those of China^[28], Finland^[17] or Germany^[29]. Nevertheless, similar mortality and severity rates were observed in populations that are geographically, culturally, culinary, and genetically similar to the Portuguese^[30].

CONCLUSION

We estimated the incidence of AP at 29.2 episodes that required hospitalization per 100000 people. The majority of our cases were found in males (68.9%) and were related to alcohol abuse (45.7%). Out of the patients we were able to find data regarding tobacco usage, a vast majority of the patients were active smokers (68.5%). Most of our patients had a mild course (54.4%), and the total mortality rate was 5.5%. Interstitial AP prevailed in our cohort (45.3%). 747.96 RON (approximately 165 EUR) was the median daily cost of hospitalization. This study's main strengths are based on the fact that is a large cohort study with over 1000 episodes and with a low bias risk of population selection regarding the fact that the episodes taken into account were consecutive AP cases of our department. The weaknesses of this study resides in the fact that is a retrospective, unicentric study that is based on medical-chart reviews that is prone to data loss between discharge and study analysis and also the lack of surgical patients. There is a need to extend this study to patients admitted in surgical departments to correctly evaluate prognosis and severity.

ARTICLE HIGHLIGHTS

Research background

Acute pancreatitis (AP) is a global burden, especially in Eastern Europe and former Soviet space. Romania although is part of Eastern Europe lacks quality epidemiological studies regarding the topics we aim in this study, like: Estimation of incidence, stratification of: Etiology, severity, outcome, morphology, estimation of cost regarding hospitalization of AP and tobacco usage prevalence in our country regarding AP cases.

Research motivation

From this study we aim to estimate the incidence, cost and tobacco usage in hospitalized AP cases and to upgrade and update former knowledge regarding: Etiology, severity, outcome, morphology of AP. Once this aim is fulfilled the data from this paper should be of use for: Medical practitioners from our country and countries that have large Romanian diaspora, medical researchers and healthcare policymakers from our country or any other international organization with a focus on this topic.

Research objectives

Main objective: Estimating the incidence was fulfilled although we were able to do that only in regard to southern Romania. Secondary objectives achieved: First estimation of AP costs in our country, first attempt to find the prevalence of tobacco usage in AP in our country. Also, we were able to update the knowledge regarding stratification. This study should be of use for a nationwide metanalysis of smaller regional studies or for a European or international metanalysis regarding this topic. This study should be also expanded with surgical patients.

Research methods

Cases drawn from BUCharest - Acute Pancreatitis Index cohort of AP and Acute-on-Chronic Pancreatitis cases, which to the best of our knowledge is the largest analysed in Romania to this date. The entire team that worked on this study, did that remotely due

to coronavirus disease 2019 pandemic restriction with the help of several online applications like: Adobe Reader, Microsoft 365 (formerly known as Microsoft Excel), Google Teams, Zoom, SPSS statistical package. We analysed data from Electronic Health Records of our facility, based on International Classification of Diseases (ICD)-10 coding of diagnostics. For the statistical analysis we used IBM SPSS v. 29.0.0.0 and we run the following tests depending on the type of variable of interest: Crosstab analysis, frequency analysis, chi-square test.

Research results

We managed to show that AP incidence total annual cost in Romania might be overestimated as stated in Global Burden of Disease study 2019 (no other recent data publicly available), this should be of great interest for healthcare policy makers in our country or other international organisation interested by this topic. In the selection of cases, we also observed that ICD-10 does not have a particular code for Acute-on-Chronic Pancreatitis, this was a limitation that was dealt through authors screening and exclusion but we consider that a code for this particular situation would be of great necessity.

Research conclusions

Our study proposes a first, as far we know, estimation regarding costs of AP in our country and also a first glance, to the best of our knowledge, regarding tobacco usage prevalence in this disease. We also managed to make a reasonable first, as far as we know, grassroots estimation of incidence of AP in our region based on the data we have at this moment.

Research perspectives

We seek in a near future to expand this study also on surgical cases and territorially as a multicentric study to be able to better estimate the current status of AP outside southern Romania.

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SIMILARITY INDEX

PRIMARY SOURCES

- 1 **Hanna Belfrage, Emiel Lankinen, Leena Kylänpää, Johanna Louhimo. "ACUTE PANCREATITIS in HELSINKI in 2016–2018: INCIDENCE, ETIOLOGY and RISK FACTORS - analysis of 1378 acute pancreatitis episodes in a Finnish normal population", Scandinavian Journal of Gastroenterology, 2022** 35 words — 1 %
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