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Assessment of Patients Monitored for Non-Biliary Acute Pancreatitis in Terms of Etiology, Prognosis, and Mortality

Nonbiliyer Akut Pankreatit Nedeniyle Takip Edilen Hastaların Etyoloji, Prognoz ve Mortalite Açısından Değerlendirilmesi

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ABSTRACT

Objectives: We planned to investigate the etiologic causes, prognosis, and mortality rates for cases diagnosed with non-biliary acute pancreatitis (AP) monitored by the internal medicine clinic.

Methods: The study included 73 patients monitored by the clinic from January 2016 to June 2021. Patients included in the assessment were investigated for age-sex, presence of chronic disease, local, and systemic complications developing linked to AP, admission to intensive care, incidence of mortality, and clinical follow-up duration.

Results: The most frequent etiological cause was idiopathic (40%), followed by hyperlipidemia (24%) and alcohol (6%). Advanced age (65 years and older) was significantly high among patients with high Ranson score (p=0.001; p<0.01). There was no correlation between sex and etiologic cause with prognosis (p>0.05). There was a significant correlation between presence of comorbid disease and high Ranson score (p=0.045; p<0.05). Among cases, 56% were observed to have recurrent AP (RAP) admissions.

Conclusion: While advanced age and presence of comorbid disease significantly contribute to the severity of AP, our study did not show an effect of etiologic factors on prognosis. RAP was observed in 56% of cases.

Keywords: Etiology; mortality; non-biliary acute pancreatitis; prognosis.

ÖZET

Amaç: Bu çalışmada, iç hastalıkları kliniğinde takip edilen nonbiliyer akut pankreatit tanılı olguların etyolojik nedenlerinin, prognozlarının ve mortalite oranlarının incelenmesi amaçlandı.

Yöntem: Çalışmaya Ocak 2016-Haziran 2021 tarihleri arasında klinik takibi yapılan 73 hasta dahil edildi. Değerlendirmeye alınan hastaların yaş, cinsiyet, kronik hastalık varlığı, akut pankreatite bağlı gelişen lokal ve sistemik komplikasyonlar, yoğun bakıma gidiş, ölüm sıklığı ve klinik takip süresi incelendi.

Bulgular: En sık etyolojik neden idiyopatik (%40) iken, bunu hiperlipidemi (%24) ve alkol (%6) izlemekte idi. İleri yaş (65 yaş ve üstü) Ranson skoru yüksek tespit edilen hastalarda daha anlamlı yüksek görüldü (p=0,001; p<0,01). Cinsiyet ve etyolojik neden ile prognoz arasında ilişki gösterilemedi (p>0,05). Ek hastalık varlığı ve yüksek Ranson skoru arasında anlamlı ilişki tespit edildi (p=0,045; p<0,05). Olguların %56'sında rekürren akut pankreatit yatışı gözlemlendi.

Sonuç: İleri yaş ve ek hastalık varlığının akut pankreatit şiddetine anlamlı katkı yaptığı görülürken, etyolojik faktörlerin prognoz üzerine etkisi çalışmamızda gösterilememiştir. Olguların %56'sında rekürren akut pankreatit görülmüştür.

Anahtar sözcükler: Etyoloji; mortalite; nonbiliyer akut pankreatit; prognoz.

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Acute pancreatitis (AP) is an acute inflammatory process in the pancreas frequently involving peripancreatic tissues and sometimes distant tissues. Severity has a broad range from mild local forms only affecting the pancreas to severe forms with multiorgan failure that may even result in mortality.[1] AP incidence has equal rates in both sexes, with frequency varying from 13–45/100,000.[2,3]

AP is characterized by acute inflammation of the pancreas and histological acinar cell destruction.[4] Inappropriate release and activation of pancreatic enzymes causes AP. Trypsin is considered to be the key enzyme for activation of pancreatic zymogens. Inappropriate activation of trypsin by trypsinogen and lack of clearance of active trypsin from the pancreas causes pancreas inflammation and then triggers the inflammatory cascade.[3,5]

AP is most commonly observed due to gallstones and excessive alcohol use. Most cases follow a mild progression, with moderate levels of fluid resuscitation, pain-nausea management and early oral feeding resulting in rapid clinical improvement. The general mortality in AP is estimated to be 5%.[6] In severe AP, mortality may increase to up to 30%.[5] In mild AP (interstitial edematous pancreatitis), there is no organ failure or local or system complications and it generally resolves in the 1st week. If there is temporary organ failure (<48 h), local complications or triggering of comorbid diseases, it is classified as moderate AP. Patients with permanent organ failure (more than 48 h) are accepted as having severe AP.[7]

In spite of the ease of access to health services, and improvements in imaging methods, treatment and care,[8] AP still continues to cause significant levels of morbidity and mortality.[9]

Aim of the Study

We planned to assess cases admitted to the internal medicine clinic due to non-biliary AP in terms of mortality, prognosis and etiology and to determine whether sex, age, etiology, and presence of chronic disease created differences in mortality and prognosis.

Methods

The study included patients with non-biliary AP diagnosis monitored by the internal medicine clinic from January 2016 to June 2021. Non-biliary AP diagnosis was made with acute onset abdominal pain or sensitivity in the upper section of the abdomen, minimum 3-fold increase in serum amylase and/or lipase, presence of findings leading to consideration of AP on ultrasonography (USG)/computer tomography/MR and exclusion of stones in the biliary and/or pancreatic ducts. When investigating etiologic causes, the condition of evaluating cases diagnosed with idiopathic pancreatitis with 2 USG sessions was sought. Biliary AP was excluded from the study due to a certain proportion requiring ERCP and debridement for treatment. Patients monitored for non-biliary AP and with stones later identified on USG or MRCP were not included in the study though they were monitored for iatrogenic pancreatitis (post-ERCP pancreatitis) by the internal medicine clinic. Cases with admission duration of <48 h were excluded from the study due to inability to use Ranson scoring. Patients over the age of eighteen were assessed and patients were investigated for age-sex, presence of chronic disease, medications used, local, and systemic complications developing linked to AP, admission to intensive care, mortality rate, and clinical follow-up duration. Admission duration longer than 7 days was assessed as "lengthened admission." Mortality and prognosis were assessed according to etiology and chronic disease. Prognosis assessment was based on the Ranson score.

Statistical Analysis

Statistical analyses used the number cruncher statistical system program. When analyzing study data, descriptive statistical methods (mean, standard deviation, median, frequency, proportion, minimum, and maximum) were used. Fit of quantitative data to normal distribution was assessed with the Kolmogorov–Smirnov, Shapiro–Wilk test, and graphical assessments. Two-group comparisons of data without normal distribution used the Mann–Whitney U test. Comparisons of qualitative data used the Pearson Chi-square test and Fisher-Freeman-Halton exact test.

Results

The study included patients monitored due to non-biliary AP in the internal medicine clinic from January 2016 to June 2021. Although seven patients were monitored for non-biliary AP, they were excluded from the study due to identification of stones in the pancreatic/biliary ducts. The study was completed with 73 cases, 46.6% women (n=34) and 53.4% men (n=39). The ages of cases varied from 22 to 89 years, with mean age of 48.67±18.30 years.

When the etiology of cases participating in the study are investigated, etiology was alcohol in 6 cases (8.2%), Caroli disease in 2 cases (2.7%), hyperlipidemia (HL) in 24 cases (32.9%), idiopathic in 40 cases (54.8%), and papilla tumor in 1 case (1.4%). There were no cases with AP linked to medication use or autoimmune AP identified in our study.

When the Ranson scoring of cases is investigated, 65.8% were mild (n=48) and 34.2% were severe (n=25).

When cases in the study are examined considering admission durations, final status and chronic-systemic complications, 68.5% had good prognosis (n=50), and 31.5% had poor prognosis (n=23).

The proportion of cases with comorbid disease was 43.8% (n=32), while 56.2% of cases did not have comorbid disease (n=41).

One patient was transferred to the intensive care unit (ICU), and two patients died. Of patients, 95% were discharged with amelioration of the AP clinic.

The admission durations of cases varied from 2 to 22 days, with mean duration 6.26±4.74 days (Table 1).

There was no statistically significant difference in sex and etiology distribution according to Ranson level (p>0.05) (Table 2).

Cases with severe Ranson score were found to have ages which were high by a significant level compared to cases with mild Ranson severity (*p=0.001; p<0.01) (Fig. 1).

The incidence of comorbid disease among cases with severe Ranson score was higher compared to cases with mild Ranson score (*p=0.045; p<0.05). The group without comorbid disease had mean Ranson score of 1.8, while the group with chronic disease had mean Ranson score of 2.5 (Fig. 2).

Table 1. Distribution of demographic and clinical characteristics

Demographic characteristics	n (%)
Gender	
Female	34 (46.6)
Male	39 (53.4)
Age (years)	
Mean±Sd	48.67±18.30
Median (Min-Max)	50 (22-89)
Clinical characteristics	
Etiology	
Alcohol	6 (8.2)
Caroli disease	2 (2.7)
HL	24 (32.9)
Idiopathic	40 (54.8)
Papillatumor	1 (1.4)
Comorbid diseases	
Yes	32 (43.8)
No	41 (56.2)
Ransonscore	
Mean±Sd	2.14±1.90
Median (Min-Max)	2 (0-10)
Mild	48 (65.8)
Severe	25 (34.2)
Hospitalization (days)	
Mean±Sd	6.26±4.74
Median (Min-Max)	5 (2-22)
≤ 7 days	54 (74.0)
> 7 days	19 (26.0)
Final outcome	
Discharge	70 (95.9)
ICU	1 (1.4)
Ex	2 (2.7)
Prognosis	
Good prognosis	50 (68.5)
Poor prognosis	23 (31.5)

Table 2. Assessment according to Ransonscore

	Ransonscore		p
	Mild (n=48)	Severe (n=25)	
Age (years)			
Mean±Sd	42.40±16.01	60.72±16.51	[a]0.001**
Median (Min-Max)	41 (22-80)	59 (28-89)	
Gender; n(%)			
Male	29 (60.4)	10 (40.0)	[b]0.097
Female	19 (39.6)	15 (60.0)	
Comorbid diseases; n(%)			
Yes	17 (35.4)	15 (60.0)	[b]0.045*
No	31 (64.6)	10 (40.0)	
Etiology; n(%)			
Alcohol	5 (10.4)	1 (4.0)	[c]0.565
Caroli disease	2 (4.2)	0 (0.0)	
HL	17 (35.4)	7 (28.0)	
Idiopathic	23 (47.9)	17 (68.0)	
Papilla tumor	1 (2.1)	0 (0.0)	

[a]Mann-Whitney U Test; [b]PearsonChi-Square Test; [c]Fisher Freeman Halton Exact Test; *p<0.05; **p<0.01.

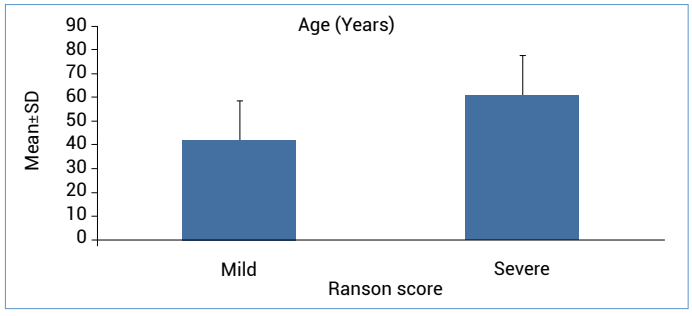

Figure 1. Age distribution according to Ranson score.

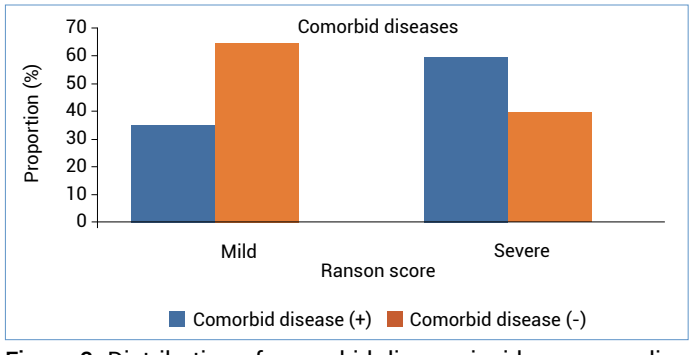

Figure 2. Distribution of comorbid disease incidence according to Ranson score.

The diagnoses for comorbid diseases of cases are shown in Table 3. The study included 73 patients with repeated admissions and the chronic diseases of 47 patients are shown in the table. As hypertriglyceridemia is a direct cause of non-biliary AP, it was not included in the table.

Discussion

The most common three causes of AP are gallstones, alcohol, and idiopathic causes, in that order.[8] The most common cause of AP in those over 60 years are gallstones, while the most common cause in cases under 60 years is HL.[10] In our study investigating the etiology of non-biliary AP, the most common cause was idiopathic for 54.8%, followed by HL for 32.9% and alcohol for 8.2%. One case had AP due to papilla tumor, and the cause was caroli disease in a patient with recurrent admissions. In our study, there was no statistically significant correlation shown between etiology and disease severity ($p>0.05$).

AP was identified in men 10–30% more frequently than in women,[11] while another study showed equal rates in both sexes.[2] Cases in our study comprised 46.6% women and 53.4% men and there was no statistically significant correlation identified between sex and Ranson score ($p>0.05$), with no correlation between sex and SP severity.

AP disrupts quality of life in the long term and causes recurrent hospitalization in many patients.[3] A retrospective analysis of patients attending hospitals in Holland identified that 17% of patients monitored for AP one time had recurrent AP (RAP) attacks.[12] A study in China identified that most cases (79.6%) with one AP attack experienced a second pancreatitis attack.[13] In our study of 73 patients admitted due to non-biliary AP, 41 (56%) were assessed as having RAP with 2 or more admissions. RAP is more frequent in alcoholic AP,[14] while in our study, the most frequent cause of RAP was idiopathic for 46%, HL for 32%, and alcohol for 12%. For 4% of those with RAP, caroli disease was identified.

Table 3. Presence of Chronic disease	Case number
DiabetesMellitus	6
Essential Hypertension	7
Chronic kidney disease	2
Chronic obstructive pulmonary disease	1
Atrial Fibrillation	1
Rheumatoid arthritis	1
Hypothyroidism	2
Alzheimer	1
Malignancy	2
No chronic disease	23
Total	47

The incidence of AP increases with age.[11] Elderly patients generally have a higher tendency to severe AP progression compared to younger patients.[15] Advanced age is accepted as an independent prognostic factor for mortality in AP.[16] The mortality of AP in patients ≥65 years was identified to be higher compared to those under 65 years with ICU admission and lengthened admission.[17,18] In young people, mortality in AP was identified as 5.3%, while mortality reaches 17% at advanced age.[10] A study investigating the effect of age on mortality rate found the mortality rate was 5.9% for patients under 50 years, while this rate was 21.3% for those aged over 75 years. Increased mortality was shown to be linked to comorbid diseases and diagnoses at time of admission, rather than complications due to the pathologic process in AP. When deaths linked to isolated AP complications are analyzed, there were no significant differences between mortality rates in young and old groups.[16] In our study, there were differences in Ranson score according to age of cases, with cases with high Ranson score identified to have significantly higher ages compared to cases with mild Ranson score ($p<0.01$). Only one AP case with complications was identified with age 65 years. Two patients who died were identified to be over 65 years. There was a significant correlation identified between presence of chronic disease and Ranson score ($p<0.05$). In the literature, there are insufficient studies related to presence of chronic disease and AP. In our study, 88% of patients aged over 65 years had minimum 1 chronic disease and it is not possible to interpret whether the severe AP that developed in these patients was due to advanced age or presence of chronic disease.

Two local complications of AP are pseudocysts and walled necrosis.[19] In our 73 patients, a total of five progressed with AP complications with pseudocyst identified in two cases, necrosis in pancreas tissue in one case and pleural effusion developing as a systemic complication in two cases. When the Ranson score of these cases is assessed, three had mild AP and two had severe AP.

The general mortality rate in severe AP varies from 5% to 17%, while it is 1.5% for mild AP.[20] A study by Gümüş et al.[21] found the mortality rate was 0.4% for mild AP and 11% for severe AP, while the study by Coşkun et al.[22] found

this rate was 3.8% for severe AP. In our study, one case was transferred to the ICU and two cases died. These cases were assessed as severe cases according to Ranson score. While mortality was not identified in mild AP cases in our study, mortality for severe AP was identified as 8%.

When patients with lengthened clinical follow-up are investigated, 7 of the 19 patients had severe non-biliary AP (36%), while 17 of the 54 cases with clinical follow-up of 2–7 days had severe AP (31%). The study by Kösekli et al.[23] identified severe AP cases had 2-times higher hospitalization and treatment costs compared to the mild edematous AP group. In our study, no significant correlation was identified between hospitalization duration and AP severity.

Study Limitations

The study included all patients abiding by the conditions monitored in the past 5 years for non-biliary AP; however, results cannot be generalized due to the inadequacy of our case numbers. Studies related to AP in general do not differentiate biliary-non-biliary types but appear to investigate data under the integrated term of AP. In spite of higher Ranson score for patients with advanced age, the lack of adequate case numbers with advanced age and presence of comorbid chronic disease with advanced age means we could not make a clear distinction about whether severe AP is due to advanced age or presence of chronic disease. All these points comprise limitations of our study.

Conclusion

Our study evaluated idiopathic AP as the most frequent etiologic cause of non-biliary AP, with HL identified as the 2nd most common cause. In severe AP cases, age was associated with poor prognosis independent of etiology ($p=0.001$; $p<0.01$). Cases with chronic disease were found to have higher Ranson score ($p=0.045$; $p<0.05$). Sex, etiologic cause, and admission duration were not associated with prognosis ($p>0.05$). Of cases, 56% were monitored for 2 or more non-biliary AP attacks and assessed as RAP. Most cases with advanced age had chronic disease and 88% of cases over 65 years in our study had at least 1 comorbid disease. There are inadequate clinical studies and data found to interpret whether age, one of the Ranson components, or presence of chronic disease cause severe AP. At this point, it is necessary to support our data and results with studies including more non-biliary AP group patients.

Disclosures

Ethics Committee Approval: Kartal Dr Lütfi Kırdar City Hospital, Decide no: 2021/514/207/4, History: 11.08.2021.

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References

1. Pandol SJ, Saluja AK, Imrie CW, Banks PA. Acute pancreatitis: Bench to the bedside. Gastroenterology 2007;132:1127–51.
2. Yadav D, Lowenfels AB. The epidemiology of pancreatitis and pancreatic cancer. Gastroenterology 2013;144:1252–61.
3. Lee PJ, Papachristou GI. New insights into acute pancreatitis. Nat Rev Gastroenterol Hepatol 2019;16:479–96.
4. Garber A, Frakes C, Arora Z, Chahal P. Mechanisms and management of acute pancreatitis. Gastroenterol Res Pract 2018;2018:6218798.
5. Whitcomb DC. Clinical practice. Acute pancreatitis. N Engl J Med 2006;354:2142–50.
6. NICE. Pancreatitis: Diagnosis and management draft scope for consultation. London, UK; 2016. Available at: https://www.nice.org.uk/guidance/ng104/documents/draft-scope
7. Leppäniemi A, Tolonen M, Tarasconi A, Segovia-Lohse H, Gamberini E, Kirkpatrick AW, et al. 2019 WSES guidelines for the management of severe acute pancreatitis. World J Emerg Surg 2019;14:27.
8. Roberts SE, Akbari A, Thorne K, Atkinson M, Evans PA. The incidence of acute pancreatitis: Impact of social deprivation, alcohol consumption, seasonal and demographic factors. Aliment Pharmacol Ther 2013;38:539–48.
9. Eland IA, Sturkenboom MJ, Wilson JH, Stricker BH. Incidence and mortality of acute pancreatitis between 1985 and 1995. Scand J Gastroenterol 2000;35:1110–6.
10. Xin MJ, Chen H, Luo B, Sun JB. Severe acute pancreatitis in the elderly: Etiology and clinical characteristics. World J Gastroenterol 2008;14:2517–21.
11. Yadav D, Lowenfels AB. Trends in the epidemiology of the first attack of acute pancreatitis: A systematic review. Pancreas 2006;33:323–30.
12. Ahmed Ali U, Issa Y, Hagenaars JC, Bakker OJ, van Goor H, Nieuwenhuijs VB, et al. Risk of recurrent pancreatitis and progression to chronic pancreatitis after a first episode of acute pancreatitis. Clin Gastroenterol Hepatol 2016;14:738–46.
13. Gao YJ, Li YQ, Wang Q, Li SL, Li GQ, Ma J, et al. Analysis of the clinical features of recurrent acute pancreatitis in China. J Gastroenterol 2006;41:681–5.
14. Yadav D, O'Connell M, Papachristou GI. Natural history following the first attack of acute pancreatitis. Am J Gastroenterol 2012;107:1096–103.
15. Losurdo G, Iannone A, Principi M, Barone M, Ranaldo N, Ierardi E, et al. Acute pancreatitis in elderly patients: A retrospective

evaluation at hospital admission. Eur J Intern Med 2016;30:88–93.
16. Fan ST, Choi TK, Lai CS, Wong J. Influence of age on the mortality from acute pancreatitis. Br J Surg 1988;75:463–6.
17. Quero G, Covino M, Fiorillo C, Rosa F, Menghi R, Simeoni B, et al. Acute pancreatitis in elderly patients: A single-center retrospective evaluation of clinical outcomes. Scand J Gastroenterol 2019;54:492–8.
18. Carvalho JR, Fernandes SR, Santos P, Moura CM, Antunes T, Velosa J. Acute pancreatitis in the elderly: A cause for increased concern? Eur J Gastroenterol Hepatol 2018;30:337–41.
19. Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, et al. Classification of acute pancreatitis--2012: Revision of the Atlanta classification and definitions by international consensus. Gut 2013;62:102–11.
20. Cavallini G, Frulloni L, Bassi C, Gabbrielli A, Castoldi L, Costamagna G, et al. Prospective multicentre survey on acute pancreatitis in Italy (ProInf-AISP): Results on 1005 patients. Dig Liver Dis 2004;36:205–11.
21. Gümüş M, Uçmak F, Önder A, Kapan M, Girgin G, Kolakan MS, et al. Our experience in acute pancreatitis: Analysis of 401 cases. Turk HPB 2009;5:60–4.
23. Coşkun BN, Tandoğan G, Eroğlu A, Karadayı D, Irak K, Cangür Ş, et al. Retrospective analysis of etiologic and prognostic factors of patients diagnosed with acute pancreatitis. J Uludağ Univ Med Fac 2012;38:67–73.
23. Kösekli MA. Retrospective analysis of 134 cases with acute pancreatitis. Master Thesis. Denizli: Pamukkale University; 2013.