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The Importance and Its Relationship of Adropin Level in Prediting the Severity of Acute Pancreatitis

Akut Pankreatitin Şiddetini Tahmin Etmede Adropin Düzeyinin Önemi ve İlişkisi

Hüseyin ŞAHİN[1], Günay NAHMADOVA[1], Sercan BIÇAKÇI[1], Nurcan BIÇAKÇI[2], Mustafa Numan ERDEM[3], Serhat ÖRÜN[1], Batuhan İlbey BAŞOL[1], Rahime Merve YANIKER[4], Aliye ÇELİKKOL[5]

[1]*Tekirdağ Namık Kemal University Faculty of Medicine, Department of Emergency Medicine, Tekirdağ, Turkey*
[2]*Tekirdağ Namık Kemal University School of Health, Department of Emergency and Disaster Management, Tekirdağ, Turkey*
[3]*Sancaktepe Şehit Prof. İlhan Varank Training and Research Hospital, Clinic of Emergency Medicine, İstanbul, Turkey*
[4]*Çorlu State Hospital, Clinic of Emergency Medicine, Tekirdağ, Turkey*
[5]*Tekirdağ Namık Kemal University Faculty of Medicine, Department of Medical Biochemistry, Tekirdağ, Turkey*

ABSTRACT

Aim: We sought an alternative marker without serum amylase-lipase test for diagnosis in acute pancreatitis (AP), a disease with a wide range of severity. In this study, we wanted to see the benefit of serum adropin levels in improving the diagnosis time in the emergency department, predicting the severity of pancreatitis, and hospitalization.

Materials and Methods: Our study is a single-center prospective study in which 39 patients with AP (≥18 years old) participated. Thirty-six patients diagnosed with AP and 36 control group admitted to the Emergency Department of Tekirdağ Namık Kemal University Hospital between March 2021 and November 2021 were included in the study. The blood samples of the patient and control groups at admission were studied by ELISA method. All patients diagnosed with AP were hospitalized and a package program called Statistical Package for the Social Sciences was used in the statistical analysis of the data obtained.

Results: In our study results; There was no statistically significant difference in adropin levels compared to the patient/control group (p>0.05). When the ROC curves of the patient/control group were examined in terms of adropin levels; It was determined that the adropin level distinction was not statistically significant (p=0.336 >0.05). At the same time, no statistically significant difference was found in terms of adropin levels according to pancreatitis types and pancreatitis score classes of the patients (p>0.05).

Conclusion: According to our study, adropin is not a significant biomarker in determining the diagnosis and severity of AP.

Keywords: Adropin, acute pancreatitis, Revised Atlanta Classification

ÖZ

Amaç: Geniş bir şiddet aralığına sahip bir hastalık olan akut pankreatitte (AP) tanı için serum amilaz-lipaz testi olmayan alternatif bir belirteç aradık. Bu çalışma ile serum adropin düzeylerinin acil serviste tanı süresini iyileştirme, pankreatittin şiddetini tahmin etme ve hastaneye yatış için faydasını görmek istedik.

Gereç ve Yöntem: Çalışmamız, 39 AP hastasının (≥18 yaş) katıldığı tek merkezli prospektif bir çalışmadır. Mart 2021-Kasım 2021 tarihleri arasında Tekirdağ Namık Kemal Üniversite Hastanesi Acil Servisi'ne başvuran AP tanısı alan 36 hasta ve 36 kontrol grubu çalışmaya dahil edildi. Hasta ve kontrol grubunun başvuruda alınan kanları ELISA yöntemi ile çalışıldı. AP tanısı alan tüm hastalar hastaneye yatırıldı ve elde edilen verilerin istatistik analizinde Statistical Package for the Social Sciences adlı paket program kullanıldı.

Bulgular: Çalışma sonuçlarımızda; hasta/kontrol grubuna göre adropin düzeyleri açısından istatistiksel olarak anlamlı farklılık yoktur (p>0,05). Hasta/kontrol grubunun adropin düzeyleri açısından ROC eğrileri incelendiğinde; adropin düzeyi ayrımının istatistiksel anlamlı olmadığı belirlenmiştir (p=0,336 >0,05). Aynı zamanda hastaların pankreatit tipleri ve pankreatit skoru sınıflarına göre de adropin düzeyleri açısından istatistiksel olarak anlamlı farklılık belirlenmemiştir (p>0,05).

Sonuç: Çalışmamıza göre adropin, AP'nin tanı ve şiddetini belirlemede anlamlı bir biyomarker değildir.

Anahtar Kelimeler: Adropin, akut pankreatit, Revize Atlanta Sınıflaması

Address for Correspondence: Hüseyin ŞAHİN MD, Tekirdağ Namık Kemal University Faculty of Medicine, Department of Emergency Medicine, Tekirdağ, Turkey
Phone: +90 533 529 37 38 **E-mail:** drhuseyinsahin@hotmail.com **ORCID ID:** orcid.org/0000-0002-8681-4034
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INTRODUCTION

Acute pancreatitis (AP) is the name given to the sudden onset of non-bacterial inflammation of the pancreas. Pancreatic proteolytic enzymes, which should be activated in the small intestine, leak into the pancreatic parenchyma and are activated there, causing autodigestion. Depending on the inflammatory condition, it can cause processes that can range from simple AP to necrotizing pancreatitis, with increased mortality[1]. Since AP is an inflammatory disease, it is not limited to itself and can also damage surrounding tissues and distant organs. Of this patient group, a single attack can develop in 15% and recurrent attacks can develop in 30%. In addition, this process may become chronic in 5-25% of patients. While approximately 80% of cases can be cured with mild symptomatic treatments, <1% of cases are fatal[2].

Adropin is a protein consisting of 76 amino acids. It was found in mice studies by Kumar et al.[3] in 2008. The most expressed adropin levels are in the tissues of the pancreas, liver, kidney, heart, brain, and cerebellar tissue, respectively[4]. Adropin has also been associated with the immune system and inflammatory processes in various organs. While doing this, it has been seen that it produces an anti-inflammatory effect by regulating energy metabolism, causing macrophage polarization and preventing apoptosis of Tregs through anti-oxidant stress[5].

The first classification system in AP was made in 1963 and many scoring systems (Ranson, APACHE-II, Atlanta, BISAP, Balthazar, EPIC) are used to determine the severity of the patient. In our study, we preferred the "Revised Atlanta Classification of Acute Pancreatitis", which was revised in 2012[6].

In this study, our aim was to determine the severity of AP by using the biomarker "adropin" and to open new doors in diagnosis and treatment by determining the relationship between its severity and adropin elevation in patients who were diagnosed with pancreatitis by clinical and serological markers (especially lipase elevation) and imaging techniques and then hospitalized. While conducting this study, patient and control groups were carefully selected by taking into account the diseases and conditions that might affect the adropin level.

MATERIALS AND METHODS

This study is a prospective, case-controlled, clinical research that was initiated after obtaining the approval of Tekirdağ Namık Kemal University Faculty of Medicine Non-Invasive Clinical Research Ethics Committee (date: 23.02.2021, protocol number: 2021.54.02.17). All participants (patient and control) participating in the study were informed about the study and written consent was obtained from the patients/relatives.

Study Population and Data Collection

The study was conducted with patients aged 18 years and above, who were admitted to Tekirdağ Namık Kemal University Hospital Emergency Service between March 2021 and November 2021 with abdominal pain, nausea and vomiting and who met the AP criteria (the presence of AP symptoms, amylase-lipase values increased at least 3 times higher than the normal value, and the presence of at least two of the radiological compatibility criteria).

All physicians in the emergency department contributed to the collection of study data between March 2021 and November 2021. Of the patients admitted to the emergency unit and met the AP criteria, antecubital vascular access was established and blood was taken from the venous route for hemogram and biochemistry, and imaging (hepatobiliary ultrasonography, abdominal computed tomography) was performed in patients with more than 3 times increase in amylase-lipase values in their blood. Before hospitalization of patients, their complaints on admission, diseases, presence of exclusion criteria, duration/time of onset of complaints, laboratory results and vital signs were recorded in data collection forms. All diagnosed patients were hospitalized.

Exclusion Criteria

Patients who were younger than 18 years old, who did not give consent to participate in the study, and who had additional diseases (heart failure, diabetes mellitus, advanced stage liver failure, advanced stage renal failure, myocardial infarction in the past 6 months, cerebrovascular event in the past 6 months, major surgery in the past 6 months, pregnancy) were excluded from the study.

Control Group and Inclusion Criteria

Patients over the age of 18 years, who were admitted to Tekirdağ Namık Kemal University Hospital Emergency Unit with non-AP findings and symptoms, who did not meet the exclusion criteria, and who volunteered to participate in the study were selected randomly [while selecting the control group, not completely healthy adults but those not having exclusion criteria and diagnosed with other conditions not requiring serious intervention (diarrhea, nausea-vomiting, vertigo, minor trauma, etc.) in the emergency unit were preferred].

Laboratory Analysis

The blood samples of the individuals included in the study were taken into an anticoagulant tube after the diagnosis was confirmed. The blood tubes were centrifuged and the plasma samples were separated. Collected samples were stored at -80 °C until the study day. On the study day, plasma samples were

brought to room temperature and studied by using the SinoGeneClon Biotech Co., Ltd. branded (catalog no: SG-11594) commercial kit. Plasma adropin levels were measured with the ELISA method.

Statistical Analysis

Statistical analyses were performed using a software called Statistical Package for the Social Sciences (SPSS) (IBM SPSS Statistics 24). Frequency tables and descriptive statistics were used to interpret the findings. Non-parametric methods were used for not normally distributed data. In accordance with non-parametric methods, the "Mann-Whitney U" test (Z-table value) method was used to compare the measurement values of two independent groups. The expected "Pearson-χ^2" crosstabs were used to examine the relationships between two qualitative variables. The Spearman's correlation coefficient was used to examine the relationship between two quantitative data that did not have a normal distribution. The Binary logistic regression: Backward LR model was used to determine the factors affecting pancreatitis risk status.

RESULTS

Demographic Characteristics

The study was conducted on a total of 72 patients, including 36 in the AP group and 36 in the control group. Thirty-seven of the patients (51.4%) were male. It was determined that the mean age of the patients was 58.22±19.13 years in the patient group and 66.17±16.07 years in the control group. There was no statistically significant relationship between the patient/control group and age classes and gender (p>0.05). The groups were independent and homogeneous in terms of the specified characteristics.

It was determined that 34 patients (94.4%) were ambulatory emergency patients, 23 (63.9%) only complained of abdominal pain, and 32 (88.9%) did not drink alcohol. It was seen that the onset of the complaint was 12 hours ago or more in 30 (83.3%) patients (Table 1).

Twenty patients (55.6%) had biliary pancreatitis, 29 (80.6%) had mild pancreatitis score, 34 (94.4%) had an emergency outcome with admission to clinic, 33 (91.7%) were discharged and 29 (80.6%) had an emergency stay of >4 hours (Table 2).

Laboratory Parameters

A statistically significant difference was found between the patient and control groups in terms of lipase values (Z=-7,300; p=0.000), and no statistically significant difference was found in terms of adropin levels (p>0.05) (Table 3).

Revised Atlanta Classification Scores and Correlations with Adropin Levels

When AP patients were evaluated according to the Revised Atlanta Classification, it was determined that 29 patients had mild pancreatitis scores and no patients with severe scores were found. There was no statistically significant difference in adropin levels according to the pancreatitis score classes of the patients (p>0.05) (Table 4).

Table 1. Distribution of demographic findings for patients

Patient (n=36)	n	%
Way of arrival to the emergency department		
By 112 ambulance	2	5.6
Outpatient application	34	94.4
Complaint		
Abdominal pain	23	63.9
Nausea-vomiting	4	11.0
Abdominal pain + nausea-vomiting	9	25.0
Alcohol use		
No	32	88.9
Yes	4	11.1
Onset of complaint		
1-3 hours	5	13.9
3-6 hours	1	2.8
>12 hours	30	83.3

Table 2. Distribution of clinical findings for patients

Patient (n=36)	n	%
Pancreatitis type		
Biliary	20	55.6
Alcoholic	2	5.6
Other (hypertriglyceridemia, drug use, infection, postERCP etc.)	14	38.8
Pancreatitis score		
Mild	29	80.6
Moderate	7	19.4
Termination of emergency care		
Admission to clinic	34	94.4
Leaving voluntarily	2	5.6
Termination of clinical care		
Discharge	33	91.7
Referal	2	5.5
Death	1	2.8
Length of stay at emergency room		
1-2 hours	1	2.8
2-3 hours	3	8.3
3-4 hours	3	8.3
>4 hours	29	80.6

ERCP: Endoscopic retrograde cholangiopancreatography

Table 3. Comparison of laboratory parameters in patient and control groups

Group variable	Patient group (n=36)		Control group (n=36)		Statistical analysis* Odds
	$\bar{X}$±SD	Median [min-max]	$\bar{X}$±SD	Median [min-max]	
Amylase	1146.17±1303.16	800.0 [129.0-7364.0]	62.03±25.19	59.0 [21.0-118.0]	Z=-7.299 **p=0.000**
Lipase	2138.19±1903.76	1696.0 [228.0-8121.0]	30.36±12.49	28.5 [14.0-60.0]	Z=-7.300 **p=0.000**
Adropin	295.50±125.85	265.9 [143.4-694.8]	331.32±190.44	282.8 [192.8-1070.8]	Z=-0.963 p=0.336
WBC	11445.83±4663.27	10250.0 [5600.0-25400.0]	8388.33±4146.35	8100.0 [10.0-18100.0]	Z=-3.104 **p=0.002**
CRP	40.56±63.17	12.5 [1.0-289.0]	43.44±51.79	24.5 [1.0-197.0]	Z=-0.530 p=0.596
Total bilirubin	2.14±2.74	0.9 [0.1-12.1]	0.57±0.51	0.4 [0.1-2.7]	Z=-3.611 **p=0.000**
Direct bilirubin	1.62±2.48	0.4 [0.1-9.3]	0.28±0.49	0.1 [0.1-2.7]	Z=-3.349 **p=0.000**
AST	178.00±235.26	98.5 [16.0-1234.0]	53.89±106.43	22.0 [10.0-497.0]	Z=-4.034 **p=0.000**
ALT	160.81±175.65	108.5 [10.0-778.0]	54.44±135.43	14.5 [3.0-634.0]	Z=-4.529 **p=0.000**
GGT	312.14±330.74	184.5 [11.0-1281.0]	63.28±140.16	23.0 [9.0-774.0]	Z=-4.027 **p=0.000**

WBC: White blood cell, CRP: C-reactive protein, AST: Aspartate aminotranferase, ALT: Alanine aminotransferase, GGT: Gamma glutamyl transferase, SD: Standard deviation, Min-max: Minimum-maxiumum

Table 4. Comparison of adropin levels according to the pancreatitis scores of patients

Patient group variable	n	Adropin levels		Statistical analysis* Odds
		$\bar{X}$±SD	Median [min-max]	
Pancreatitis score				
Mild	29	282.26±113.42	261.6 [143.4-629.5]	Z=-1.299
Moderate	7	350.35±167.31	318.1 [186.7-694.8]	p=0.194

SD: Standard deviation, Min-max: Minimum-maxiumum

DISCUSSION

AP is a gastrointestinal system disease, which is a frequent cause of admission to the emergency department and has a relatively high mortality risk (ranging between 3% and 17%)[7]. It is a disease that is mostly diagnosed in emergency services because of the sudden onset, nausea-vomiting, and belt-like abdominal pain that radiates to the back. Mortality and morbidity vary according to risk factors, presence of comorbid diseases and complications. The rapid onset of treatment is of great importance in the prognosis. The clinical use of rapid diagnostic tools in order to reach rapid treatment brings with it an increase in research for new and rapid diagnostic markers.

Patients with a diagnosis of AP included in our study were grouped as mild, moderate and severe AP patients using the Revised Atlanta Classification. In a retrospective study of 250 patients by Pongprasobchai et al.[8], disease severity was determined using the Modified Atlanta Criteria, and 72% of the patients were found to have mild AP, 16% to have moderate AP, and 12% to have severe AP. In our study, 80.6% of the patients were mild and 19.4% were moderate. There was no patient who met the criteria for severe AP. Similar to both studies, it is seen that the majority of cases include mild and moderate AP. The absence of severe AP patients may be related to rapid diagnosis and rapid onset of treatment.

Although it may vary according to countries and cultures, in general, the most common causes of FP are found to be gallstones by 40-60%, alcohol by 10-20%, and other causes by 5-10% (hypertriglyceridemia, drugs, trauma, infection,

anatomical, genetic, autoimmune and iatrogenic causes)[7,9]. In the study of Tamer et al.[10], it was found that AP was caused by biliary and idiopathic factors at the rates of 66% and 31%, respectively. In our study, similar to the study of Tamer et al.[10], we found that 55.6% (n=20) of AP developed from biliary causes, 5.6% (n=2) from alcoholic causes, and 38.8% (n=14) from other causes. Hiding alcohol use in the history, inability to perform lipid profile examinations in the emergency department, and limitations in accessing advanced examination methods such as magnetic resonance cholangiopancreatography (MRCP) may have led to limitations in these evaluations. In addition, although it is thought that the use of >50 g of alcohol per day triggers alcoholic pancreatitis, the cause remains idiopathic in <5% of chronic alcoholics[7].

In our study, no statistically significant relationship was found between the patient/control group, and age classes and gender (p>0.05). The groups were found to be independent and homogeneous in terms of the specified characteristics. In the study of Lankisch et al.[11], investigating the relationship between AP severity and gender, similar results were found, and no correlation was found between the disease and gender. In the multicenter study conducted by Uomo et al.[12] with 1173 patients, no significant difference was found in terms of mortality in AP between males and females. Based on these findings, it can be said that there is no statistically significant difference between the genders in terms of AP mortality.

In our study, it was determined that the mean age was 58.22±19.13 years in the patient group and 66.17±16.07 years in the control group. There are many studies in the literature investigating the relationship between age and AP severity/mortality. Studies have shown that increased age worsens the outcomes of AP and increases the risk of mortality. In the study of Carvalho et al.[13], it was revealed that increasing age was associated with temporary/permanent organ failure, length of stay in the clinic/intensive care unit, increased need for interventional procedures, and high mortality. Koziel et al.[14] found that mortality was significantly increased in patients over the age of >65 years, particularly in patients over the age of >80 years.

In a study conducted by Yadav et al.[15] on 7456 patients diagnosed with AP for the first time between 1995 and 2005, it was determined that 45% of the patients were male and 55% were female, and the mean age was 58±20 years. In our study, although the sample size was much smaller and was performed without considering the initial diagnosis, 53% of the patients were male and 47% were female. In addition, our mean age in our patient group was found to be 58±20 years, similar to that study. Although the information on the global epidemiology of AP varies, there are studies showing that there is no statistically significant difference between men and women and that the disease predominantly affects middle-aged or older people[16-18].

Serum pancreatic enzyme measurement is the "gold standard" for the diagnosis of AP[19]. In an AP episode, amylase, lipase, elastase, and trypsin are simultaneously released into the bloodstream, but clearance may vary depending on the time of blood collection. AP is the main cause of the increase in lipase. Amylase is an enzyme secreted from the salivary glands, small intestine, ovaries, adipose tissue and skeletal muscles as well as the pancreas. In AP, serum lipase remains elevated longer than serum amylase[20]. While amylase and lipase values were found to be higher in biliary pancreatitis, no correlation was found between adropin level and pancreatitis type. When the patient/control groups were compared in terms of amylase-lipase and adropin levels, it was seen that amylase-lipase values increased significantly in the patient group, but there was no such increase or significant change in adropin levels.

Study Limitations

Although adropin is mostly secreted from the pancreas in the body, no literature research has been found on how adropin level is affected by inflammatory changes in the pancreas. In our study, which was planned in this direction, limiting factors such as the small number of patients, inconsistencies in the history (especially regarding alcohol use), inability to perform lipid profile tests in the emergency department, and dificulties in accessing advanced examination methods such as MRCP were encountered.

CONCLUSION

It was determined that the difference in adropin level between the patient and control groups was not statistically significant. No statistically significant difference was found in terms of adropin levels according to pancreatitis types and pancreatitis score classes. We believe that the use of adropin as a biomarker in the diagnosis of AP and in determining its severity is not suitable for now. For this, more comprehensive and advanced studies are needed.

Ethics

Ethics Committee Approval: The study was approved by the Tekirdağ Namık Kemal University Faculty of Medicine Non-Invasive Clinical Research Ethics Committee (date: 23.02.2021, protocol number: 2021.54.02.17).

Informed Consent: Consent form was filled out by all participants.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: G.N., B.İ.B., Concept: H.Ş., S.B., N.B., Design: H.Ş., S.B., M.N.E., Data Collection or Processing: G.N., B.İ.B., R.M.Y., Analysis or Interpretation: S.Ö., R.M.Y., A.Ç., Literature Search: H.Ş., M.N.E., S.Ö., R.M.Y., Writing: H.Ş., G.N., N.B.

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REFERENCES

1. Barreto SG, Windsor JA. Surgical Diseases of the Pancreas and Biliary Tree. 2018.
2. Tintinalli JE. Pancreatitis and Cholecystitis. In: Tintinalli's Emergency Medicine. 2020:508-16.
3. Kumar KG, Trevaskis JL, Lam DD, Sutton GM, Koza RA, Chouljenko VN, et al. Identification of Adropin as a Secreted Factor Linking Dietary Macronutrient Intake with Energy Homeostasis and Lipid Metabolism. Cell Metab. 2008;8:468-81.
4. Aydin S. Presence of adropin, nesfatin-1, apelin-12, ghrelins and salusins peptides in the milk, cheese whey and plasma of dairy cows. Peptides. 2013;43:83-7.
5. Zhang S, Chen Q, Lin X, Chen M, Liu Q. A Review of Adropin as the Medium of Dialogue between Energy Regulation and Immune Regulation. Oxid Med Cell Longev. 2020;2020:3947806.
6. 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.
7. Binicier ÖB, Patır DÇ. Treatment of Acute Pancreatitis. Turkiye Klin J Intern Med. 2021;6:22-38.
8. Pongprasobchai S, Vibhatavata P, Apisarnthanarak P. Severity, Treatment, and Outcome of Acute Pancreatitis in Thailand: The First Comprehensive Review Using Revised Atlanta Classification. Gastroenterol Res Pract. 2017;2017:3525349.
9. Garber A, Frakes C, Arora Z, Chahal P. Mechanisms and Management of Acute Pancreatitis. Gastroenterol Res Pract. 2018;2018:6218798.
10. Tamer A, Yaylacı S, Demirsoy H, Nalbant A, Genç A, Demirci H, et al. Retrospective Analyses Of The Acute Pancreatitis. Sakarya Med J. 2011;1:17-21.
11. Lankisch PG, Assmus C, Lehnick D, Maisonneuve P, Lowenfels AB. Acute pancreatitis: does gender matter? Dig Dis Sci. 2001;46:2470-4.
12. Uomo G, Pezzilli R, Gabbrielli A, Castoldi L, Zerbi A, Frulloni L, et al. Diagnostic assessment and outcome of acute pancreatitis in Italy: results of a prospective multicentre study. ProInf-AISP: Progetto informatizzato pancreatite acuta, Associazione Italiana Studio Pancreas, phase II. Dig Liver Dis. 2007;39:829-37.
13. 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.
14. Koziel D, Gluszek-Osuch M, Suliga E, Zak M, Gluszek S. Elderly persons with acute pancreatitis - specifics of the clinical course of the disease. Clin Interv Aging. 2018;14:33-41.
15. Yadav D, O'Connell M, Papachristou GI. Natural history following the first attack of acute pancreatitis. Am J Gastroenterol. 2012;107:1096-103.
16. Xiao AY, Tan ML, Wu LM, Asrani VM, Windsor JA, Yadav D, et al. Global incidence and mortality of pancreatic diseases: a systematic review, meta-analysis, and meta-regression of population-based cohort studies. Lancet Gastroenterol Hepatol. 2016;1:45-55.
17. Pendharkar SA, Mathew J, Petrov MS. Age- and sex-specific prevalence of diabetes associated with diseases of the exocrine pancreas: A population-based study. Dig Liver Dis. 2017;49:540-4.
18. Pendharkar SA, Mathew J, Zhao J, Windsor JA, Exeter DJ, Petrov MS. Ethnic and geographic variations in the incidence of pancreatitis and post-pancreatitis diabetes mellitus in New Zealand: a nationwide population-based study. N Z Med J. 2017;130:55-68.
19. Toouli J, Brooke-Smith M, Bassi C, Carr-Locke D, Telford J, Freeny P, et al. Guidelines for the management of acute pancreatitis. J Gastroenterol Hepatol. 2002;17(Suppl):15-39.
20. 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.