



ARAŞTIRMA / RESEARCH

Use of amylase tests in emergency department

Acil serviste amilaz testlerinin kullanılması

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Abstract

Purpose: The aim of this study was to establish how frequent the amylase test was ordered and to determine its effectiveness in patients that apply to the emergency department.

Materials and Methods: Among the 32,922 patients who had amylase tests ordered, the data from the files of 4,318 patients with high amylase levels (>100 IU/L) were evaluated. The remaining 1,543 patients were included in the study. The demographic data, laboratory results, definitive diagnoses and medication data of the patients were evaluated.

Results: Amylase tests were ordered in 15.1% of the patients that applied to the emergency department, and high amylase levels were detected in 1.98%. The incidence of acute pancreatitis diagnosed in the emergency department was identified as 60 in 100.000. When the serum amylase cut-off value was taken as three times greater than the normal upper limit, it was identified that the sensitivity and specificity of amylase in diagnosing acute pancreatitis was 85.4% and 98.0% when distinguishing patients with diseases known to increase amylase. Sensitivity and specificity of amylase in diagnosing acute pancreatitis was 85.4% and 95.3% when distinguishing patients with no diseases known to increase amylase or no medication use.

Conclusion: Besides acute pancreatitis, increased amylase levels are also observed in other gastrointestinal, gynecological, cardiovascular, neurological diseases and renal dysfunction. Ordering amylase tests based on the patients' clinic will reduce ordering unnecessary tests in emergency departments.

Keywords: Amylase, emergency, pancreatitis, drugs, laboratory tests.

Öz

Amaç: Çalışmamızda acil servise başvuran hastalarda ne sıklıkla amilaz testi istendiğini ve bu testin etkinliğini göstermeyi amaçladık.

Gereç ve Yöntem: Amilaz tetkiki istenilen 32.922 hastadan amilaz yüksekliği (>100 IU/L) saptanan 4318'nin dosya bilgileri incelendi. Geriye kalan 1543 hasta çalışmaya dahil edildi. Hastaların demografik verileri ile laboratuvar değerleri, hastaların nihai tanıları ve ilaç bilgileri değerlendirildi.

Bulgular: Acil servise başvuran hastaların %15,1'inden amilaz tetkiki istenilmiş olup, %1,98'inde amilaz yüksekliği saptandı. Acil servisteki tanı alan akut pankreatit insidansı 100.000'de 60 olarak saptandı. Serum amilaz kestirim değeri normalin üst limitinin 3 kat ve üzeri esas alındığında amilazın akut pankreatit tanısı koymadaki sensitivitesi ve spesifitesi amilaz düzeyini yükselttiği bilinen hastalıklarla ayırmada %85,4 ve %98,0 idi. Amilazın akut pankreatit tanısı koymadaki sensitivitesi ve spesifitesi amilazı yükselttiği bilinen bir hastalık veya ilaç kullanımı olmayan hastalarla ayırımında %85,4 ve %95,3 olarak saptandı.

Sonuç: Amilaz yüksekliği akut pankreatit ile beraber diğer gastrointestinal, jinekolojik, kardiyovasküler, nörolojik hastalıklar ve renal fonksiyon bozukluklarında da görülmektedir. Acil servislerde hastalardan kliniğine göre amilaz tetkiki istenilmesi gereksiz tetkik istenilmesini önleyecektir.

Anahtar kelimeler: Amilaz, acil tıp, pankreatit, ilaçlar, laboratuvar testleri

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INTRODUCTION

Amylase is a test frequently ordered in patients that apply to the emergency department with complaints of abdominal pain, nausea, or vomiting¹⁻³. The diagnosis of acute pancreatitis is based on serum amylase levels three times greater than the normal levels and abdominal pain starting from the epigastric area wrapping around the waist and radiating to the back. Imaging methods support the diagnosis and show the severity of pancreatitis⁴. Besides the pancreas, amylase is secreted from a variety of organs such as salivary glands, the liver, biliary ducts, the duodenum, the stomach, the esophagus, lungs, the heart, and fallopian tubes and is ectopically produced by many of the solid organs and hematological malignancies. Therefore, it is being reported that hyperamylasemia may also be detected in many extrapancreatic diseases such as mumps, parotitis, peptic ulcer perforation, perforated appendicitis, intestinal obstruction, mesenteric infarction, pulmonary embolism, pneumonia, myocardial infarction, malignancy, lymphoma and tubo-ovarian pathologies⁵⁻⁹. Besides the fact that amylase increases in such a variety of clinical conditions, increases related to medications are also described¹⁰⁻¹². However, the patient overcrowding and the inability to take adequate histories due to communication challenges in the emergency department have placed serum amylase levels among routine tests ordered in the emergency department to reduce the duration of stay under observation. In parallel with our observation, we aimed to demonstrate the effect of serum amylase levels on the diagnoses made and to prevent unnecessary testing in patients that apply to the emergency service.

MATERIALS AND METHODS

The study was launched after obtaining ethical approval (Trial Registration Number: ANEAH.EK.2014/96) from the Health Sciences University Adana Numune Research and Training Hospital. Patient files of the patients that were 18 years-of-age or older that applied to the emergency department hospital between 1 April and 31 October 2015 were screened retrospectively. Within this time frame, serum amylase levels were obtained for 32,922 of the 217,907 patients that had applied to the emergency department. Among the 32,922 patients who had amylase tests ordered, the data from the files of 4,318 patients with high amylase levels (>100

IU/L) were evaluated. Among the 2,100 patients whose file information was accessible completely, foreign nationals, pregnant women, trauma patients, oncology patients, and intoxication patients were excluded from the study (the numbers were 168, 287, 189, 71, and 10, respectively). The remaining 1,543 patients were included in the study. The blood samples obtained in the emergency observation room were analyzed in the laboratory in a ROCHE Cobas Integra 800 device using an AMYL-2 kit using the colorimetric enzymatic method and normal limits were between 28-100 U/L. It was identified that 4,318 patients had serum amylase levels higher than 100 IU/L. The examination findings, accompanying diseases, medications being used, demographic features such as age and gender, laboratory values, and patient diagnoses at admission and discharge were sought and recorded from the patients' emergency observation forms.

Statistical analysis

The SPSS (22.0) program was used in the analyses. The distribution of the data was assessed using the Kolmogorov-Smirnov test. The Kruskal-Wallis and Mann-Whitney-U tests were used in the analysis of quantitative data. The chi-square test was applied in the analysis of qualitative data. The effect level and cut-off value were investigated using ROC curves. Statistical significance was accepted as $p \leq 0.05$.

RESULTS

Serum amylase tests were ordered in 32,922 (15.1%) of the 217,907 patients that applied to the emergency department between 1 April and 30 October. The amylase level was higher than 100IU/L in 4,318 (1.98%) of the patients in which amylase tests were ordered. Among the 32,922 patients who had amylase tests ordered, the data from the files of 4,318 patients with high amylase levels (>100 IU/L) were evaluated. Among the 2,100 patients whose file data was accessible completely, foreign nationals, pregnant women, trauma patients, oncology patients, and intoxication patients were excluded from the study (the numbers were 168, 287, 189, 71, and 10, respectively). The remaining 1,543 patients were included in the study. Among the patients with high amylase levels, 817 (52.9%) were female, and the mean age of the patients was 56.9 ± 19.7 .

Acute pancreatitis was diagnosed in 131 (8.5%) of the patients with increased amylase levels. The incidence

of pancreatitis during the time frame stated was identified as 60 in 100,000. Among these patients, 71.8% were biliary, and 28.2% were non-biliary.

In 43.0% of the patients with increased amylase levels, extrapancreatic causes of increased amylase values were identified. (Table 1) Among the 663

patients in this group, 148 had 2 diagnoses, and 38 had 3 diagnoses. The most frequently diagnosed diseases were chronic kidney disease (n: 94, 10.6%), pneumonia (n: 89, 10.0%), acute coronary syndrome (n: 81, 9.1%), acute kidney injury (n: 75, 8.5%) and acute gastroenteritis (n: 73, 8.2%) in a descending order.

Table 1. Diagnosis of the patients with diseases known to increase amylase other than pancreatitis.

Group II Diagnosis	n	%		n	%		n	%
Chronic Kidney Disease	94	10.6	Hyperpotassemia	8	0.9	Hepatorenal Syndrome	2	0.2
Pneumonia	89	10.0	Ischemic CVE	8	0.9	A-V Nodal Rhythm	2	0.2
Acute Coronary Syndrome	81	9.1	Pelvic Inflammatory Disease	7	0.8	Aortic Dissection	2	0.2
Acute Kidney Injury	75	8.5	Hypoglycemia	6	0.7	Uremic Gastropathy	2	0.2
Acute Gastroenteritis	73	8.2	Acute Appendicitis	6	0.7	Ovarian Cyst Rupture	2	0.2
Urinary System Infections	49	5.5	Hypertensive Pulmonary Edema	5	0.6	Ovarian Torsion	2	0.2
Renal Colic	45	5.1	Cardiac Arrest	4	0.5	Terminal Ileitis	2	0.2
Pulmonary Edema	32	3.6	Post-op Complications	4	0.5	Asthma Attack	2	0.2
Anemia	21	2.4	Parotitis	4	0.5	Gastroesophageal Reflux	1	0.1
COPD Attack	18	2.0	Atrial Fibrillation	3	0.3	Hypocalcemia	1	0.1
Non-specific Abdominal Pain	17	1.9	Acute Bronchitis	3	0.3	Tick Bite	1	0.1
Cholelithiasis	16	1.8	Atypical Chest Pain	3	0.3	Anaphylaxis	1	0.1
Hepatic Cirrhosis	14	1.6	Sepsis	3	0.3	Aneurysm of Dialysis Fistula	1	0.1
Scorpion Sting	14	1.6	Hemorrhagic CVE	3	0.3	Intraabdominal Abscess	1	0.1
Cholecystitis	13	1.5	Abdominal Aorta Aneurysm	3	0.3	Diabetic Ketoacidosis	1	0.1
Urolithiasis	12	1.4	Sickle Cell Anemia	3	0.3	Duodenal Ulcer Perforation	1	0.1
Congestive Heart Failure	11	1.2	Dysmenorrhea	3	0.3	Nephrotic Syndrome	1	0.1
Cholelithiasis	11	1.2	Vesical Globus	3	0.3	Cholangitis	1	0.1
Hypernatremia	11	1.2	Peptic Ulcer Perforation	3	0.3	Leptospirosis	1	0.1
Upper GIS Bleeding	10	1.1	Epileptic Attack	2	0.2	Nephrostomy Dislocation	1	0.1
Transient Hypertensive Attack	9	1.0	Transient Hypotensive Attack	2	0.2	Ovarian Hyperstimulation Syndrome	1	0.1
Hyponatremia	9	1.0	Epistaxis	2	0.2	Tuberculous Peritonitis	1	0.1
Alcohol Intake	8	0.9	Hyperglycemia	2	0.2	Uremic Encephalopathy	1	0.1
Hepatic Encephalopathy	8	0.9	Rapid Ventricular Response AF	2	0.2	MODS	1	0.1

Ileus	8	0.9	Hypopotassemia	2	0.2	Acute Adrenal Failure	1	0.1
Ovarian cyst	8	0.9	Inguinal Hernia	2	0.2	Acute Hepatitis	1	0.1
Complications of Dialysis Catheters	8	0.9	Symptomatic Bradycardia	2	0.2			

COPD: Chronic Obstructive Pulmonary Disease, CVE: Cerebrovascular Event, AF: Atrial Fibrillation, A-V: Atrioventricular, MODS: Multiple Organ Dysfunction Syndrome, GIS: Gastrointestinal System

Among the 749 (48.5%) patients that had no diseases known to increase amylase, 417 (27.0%) were on a medication, and 332 (21.5%) were not on any medications and did not consume alcohol. Most of the patients used more than one medication simultaneously. The most frequently used

medications were identified as antiepileptics (n:111, 14.8%), iron preparations (n: 109, 14.6%), antibiotics (n:99, 13.2%), steroids (n:104, 13.9%), beta agonists (n:100, 13.4%), angiotensin converting enzyme inhibitors (n:99, 13.32%) in a descending order. (Table 2).

Table 2. The medications used by patients with no diseases known to increase amylase.

Group III					
Medications Used	n	%		n	%
Antiepileptics	111	14.8	Hormones	19	2.5
Iron Deficiency Medications	109	14.6	Anti-dementia	18	2.4
Antibiotics	108	14.4	Muscle Relaxants	16	2.1
Steroids	104	13.9	Anti-vertigo Medications	16	2.1
Beta Agonists	100	13.4	Other Antihypertensive	13	1.7
ACE Inhibitors	99	13.2	Leukotriene Receptor Antagonists	13	1.7
Diuretics	96	12.8	Xanthines	13	1.7
Beta Blockers	90	12.0	Cardiac Glycosides	13	1.7
Angiotensin II Antagonists	88	11.7	Vitamine K Antagonists	12	1.6
Antithrombotics	74	9.9	GISMDs	12	1.6
Non-steroid Anti-Inflammatory Drugs	73	9.7	Minerals	12	1.6
Antidepressants	54	7.2	Antihistamines	11	1.5
Calcium Channel Blockers	50	6.7	Bisphosphonates	11	1.5
Insulins	50	6.7	Alfa Antagonists	10	1.3
Oral Antidiabetics	47	6.3	Phosphodiesterase Inhibitors	10	1.3
Anti-lipids	37	4.9	Alfa + Beta Blockers	10	1.3
Proton Pump Inhibitors	31	4.1	Dopaminergics	9	1.2
Anticholinergics	26	3.5	Other Cardiovascular Medications	4	0.5
Vitamins	22	2.9	Other Medications	3	0.4
Cardiac Vasodilators	19	2.5			

ACE: Angiotensin Converting Enzyme, GISMDs: Gastrointestinal System and Metabolism Drugs,

When the patients with acute pancreatitis were grouped in group 1, the patients with diseases known to increase amylase other than pancreatitis in group 2, and patients with no diseases known to increase amylase in group 3, a statistically significant difference was detected between the amylase levels of Group 1 and Group 2. ($p < 0.001$, sensitivity: 85.4%, specificity: 95.3%, negative cut-off: 97.1%). The highest amylase cut-off value was 300 IU/L. (Figure 1) When the cut-off value was taken as 100 IU/L, sensitivity was 100%, specificity was 0.2%, positive predictive value was 16.4%, negative predictive value

was 100%. Statistically significant difference was identified between the amylase levels of Group 1 and Group 3 ($p < 0.001$, sensitivity: 85.4%, specificity: 98%, negative predictive value: 97.5%, positive predictive value: 88.1%). The highest amylase cut-off value was 300 IU/L. (Figure 2) Sensitivity was 100%, specificity was 0.4%, positive predictive value was 14.8%, negative predictive value was 100% when the cut-off value was taken as 100 IU/L. Although cut-off value 100 IU/L increased sensitivity and the negative predictive value, it showed very low specificity. There was no statistically significant

difference between the amylase levels of the Group 2 and 3 ($p > 0.05$). When Group 3 was separated into medication users and non-users, no statistically significant difference was detected between the amylase levels of groups.

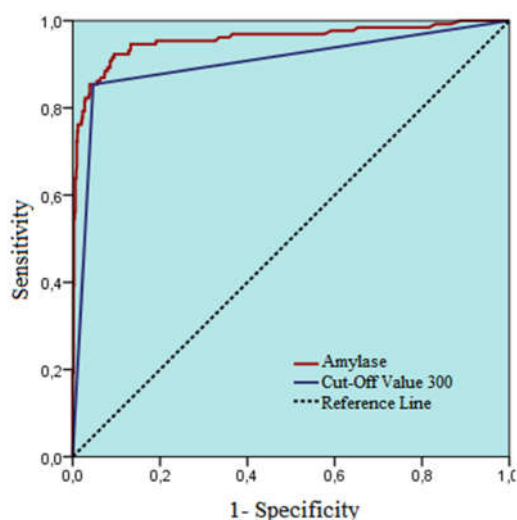


Figure 1. ROC Curve (Group 1 and 2)

When the biochemistry tests of patients with amylase levels 300 IU/L or higher and lower than 300 IU/L were compared, it was seen that the AST, ALT, ALP, GGT, total and direct bilirubin levels were significantly higher in patients with amylase levels ≥ 300 IU/L. ($p < 0.05$).

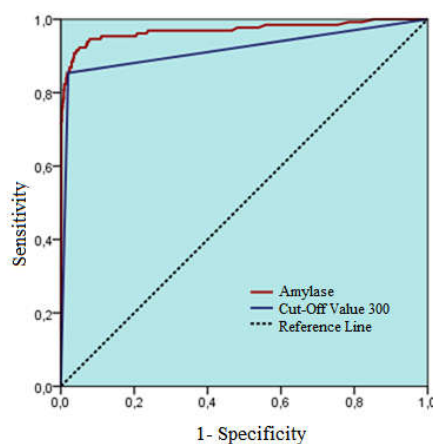


Figure 2. ROC Curve (Group 1 and 3)

DISCUSSION

The global incidence of acute pancreatitis is between 4.9 and 73.4 in 100,000¹³⁻¹⁴. As for our study, it was identified as 60 in 100,000. We could not find any studies on the frequency of ordering serum amylase levels in patients that apply to the emergency department except the study conducted by Lang and colleagues. In this study, it was reported that amylase tests were ordered in 794 (8.8%) of the 9,000 patients applied to the emergency department throughout 4 months and increased amylase levels were detected in 69 (0.76%) patients¹⁵. In our study, amylase tests were ordered at a rate of 15.1%, and increased amylase levels were identified in 1.98% of the patients. The evaluation of the group with increased amylase levels showed that 8.5% was diagnosed with acute pancreatitis. Amylase test is usually ordered in patients with non-specific abdominal complaints and it should be considered in patients with unknown abdominal pain. It is essential to support the diagnosis of acute pancreatitis with the amylase level in patients with typical abdominal pain. Typical

abdominal pain is essential for the differential diagnosis of acute pancreatitis in the emergency evaluation¹⁶⁻¹⁷. In addition, other gynecological, cardiovascular, neurological, or renal diseases that increase amylase levels with or without abdominal pain other than acute pancreatitis also exist^{5-6, 8, 18-20}. In our series, these diseases were identified in 663 (43.0%) of the patients. Therefore, especially in the patients with serum amylase levels < 300 IU/L, pancreatitis as well as non-pancreatic diseases should be considered in the differential diagnosis. Evaluating these patients with a thorough anamnesis and physical examination could have prevented ordering amylase tests during the diagnostic process. However, patient overcrowding and the insufficiency of the number of doctors present to attend patients, and the effort to shorten the patient's wait in triage in the emergency department may explain why the amylase test was ordered when not indicated.

It is recommended to take amylase levels greater than three times the normal limit as reference in the diagnosis of acute pancreatitis²¹⁻²³. In our study, we also demonstrated that the specificity and sensitivity

of amylase in diagnosing acute pancreatitis increased when the highest cut-off amylase level is taken as 300 IU/L, three times greater than the normal limit. When the cut-off value of amylase level was taken as 100 IU/L (upper limit of normal value) sensitivity and the negative predictive value increased but specificity decreased. Albeit the sensitivity and negative predictive value of amylase level is precious, differential diagnosis of acute pancreatitis is more important. In the presence of these data, cut-off value of serum amylase in the discriminator role should be taken higher as reported before.

Different medications that cause isolated increased serum amylase levels have been reported in the literature¹⁰⁻¹². When the patients that did not have any diseases known to increase serum amylase levels were grouped patients on medications and patients that are not on any medications, no significant difference was identified between their amylase levels. As the study design was retrospective and the medications were determined from the records, we could not conclude that the drugs did not make any difference on amylase levels exactly. Due to the use of multiple medications and the heterogeneity of the medications, it was not possible to evaluate their effects on the increased amylase levels clearly. The main limitations in our study are being carried out in a single center retrospectively and absence of gold standard test for the diagnosis of pancreatitis.

To conclude, if the serum amylase levels are greater than three times the normal level, this is significant and specific in the diagnosis of acute pancreatitis. Ordering amylase tests in 15.1% of the patients applied to emergency department is an indicative of overutilization. Although our study results belonging to a single center renders them inadequate to be generalized, they emphasize the importance of ordering amylase tests only when clinically required.

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