HAFİF DERECELİ PANKREATİT OLGULARININ TANISINDA LİPAZ/AMİLAZ ORANI VE ORTALAMA PLATELET HACMİ NE KADAR GÜVENİLİRDİR?

How Reliable are Lipase/Amylase Ratio and Mean Platelet Volume in the Diagnosis of Mild Pancreatitis Patients?

Emin UYSAL[1], Yahya Ayhan ACAR[2], Süleyman SOLAK[1], Mehmet SAM[1], Hatike BABAYİĞİT HANCER[3], Esra COŞKUNTUNCEL BİLGİ[4]

[1]Department of Emergency Medicine Bagcilar Training and Research Hospital, Istanbul, Turkey

[2]Department of Emergency Medicine Gulhane Training and Research Hospital, Ankara, Turkey

[3]Department of Internal Medicine Bagcilar Training and Research Hospital, Istanbul, Turkey

[4]Department of Radiology Bagcilar Training and Research Hospital, Istanbul, Turkey

Emin UYSAL, MD
Yahya Ayhan ACAR, MD
Süleyman SOLAK, MD
Mehmet SAM, MD
Hatike BABAYİĞİT HANCER, MD
Esra COŞKUNTUNCEL BİLGİ, MD

İletişim:
Emin UYSAL, MD
Department of Emergency Medicine Bagcilar Training and Research
Hospital, Istanbul
Tel: +90530 5431937
e-mail:
dreminuysal@hotmail.com

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ÖZET

Amaç: Bu çalışmanın amacı pankreatit tanısında lipaz/amilaz oranı ve ortalama platelet hacminin kullanılabilirliğini değerlendirmektir.

Materyal ve Metot: Bu çalışma, üçüncü basamak bir sağlık kuruluşunun erişkin yoğun bakım kliniğinde 1 Ocak 2010 ile 31 Aralık 2015 tarihleri arasında yatan hastalar arasında retrospektif olarak yapılmıştır. Hastaların amilaz, lipaz ve ortalama platelet hacim değerleri kaydedilmiştir. Baltazar skoru 1 ila 3 arasındaki hafif dereceli pankreatit olguları pankreatit olmayanlarla karşılaştırılmıştır.

Bulgular: Çalışmaya toplam 398 (267 pankreatit, 132 pankreatit olmayan kontrol) hasta dâhil edilmiştir. Ortalama yaş 58.87±18.65 iken hastaların 245 (%61.6) tanesi kadındı. Sonuçlarımıza göre, amilaz ve lipaz değerleri hem pankreatit (sırasıyla 1779,44±1214,46 ve 1932,68±1642,06) hem de kontrol (sırasıyla 1320,55±1252.24 ve 1719,81±1501,60) gruplarında yüksekti. Lipaz/amilaz oranlarında iki grup arasında anlamlı bir fark vardı (p=0.006). Pankreatit tanısında lipaz/amilaz oranının 1'den büyük olduğu değerler için duyarlılığı %50, özgünlüğü ise %67 olarak hesaplandı. Ortalama platelet hacmi pankreatit ve kontrol gruplarında farklılık göstermedi (p=0,101).

Sonuç: Lipaz/amilaz oranı pankreatit tanısında faydalı olabilir fakat ortalama platelet hacminin bu konuda değeri sınırlıdır.

Anahtar Sözcükler: *Pankreatit; Amilaz; Lipaz; Ortalama platelet hacmi*

ABSTRACT

Aim: The aim of this study is to evaluate the utility of lipase/amylase ratio and mean platelet volume in the diagnosis of pancreatitis.

Material and Method: This is a retrospective study conducted in a tertiary hospital's adult intensive care unit between January 1st, 2010 and December 31st, 2015. Amylase, lipase and mean platelet volume results were recorded. Mild pancreatitis patients which have Balthazar score between 1 and 3 were compared to patients with Balthazar score of 0.

Results: A total of 398 (267 pancreatitis, 132 non pancreatitis) patients were enrolled to the study. Mean age was 58.87±18.65 and 245 (61.6 %) of the subjects were female. Our results showed that mean amylase and lipase levels were high for both higher Balthazar score (1779.44±1214.46; 1932.68±1642.06, respectively) and Balthazar score of 0 (1320.55±1252.24; 1719.81±1501.60, respectively) groups. There was a significant difference for lipase/amylase ratio between two groups (p=0.006). The sensitivity and specificity to predict Balthazar score in adult pancreatitis patients with lipase/amylase ratio at>1.0 were 50% and 6 %, respectively. Mean platelet volume did not show any difference according to Balthazar score levels (p=0.101).

Conclusion: Lipase/amylase ratio can be beneficial for the prediction of the severity of pancreatitis but mean platelet volume does not appear to be valuable marker in that manner.

Keywords: *Pancreatitis; Amylase; Lipase; Mean platelet volume*

INTRODUCTION

Pancreatitis is an important clinical condition in the differential diagnosis of abdominal pain in the emergency department with an increasing incidence and causing significant burden on intensive care unit (ICU) resources (1, 2). Besides history, signs and symptoms, and physical examination, diagnosis is based on laboratory and radiologic imaging (3). In the laboratory analysis, elevated white blood cell (WBC), amylase, and lipase have been associated with pancreatitis but these markers showed different specificity and sensitivity values. Lipase/amylase ratio, platelet count, coagulation parameters and mean platelet volume (MPV) have been reported as inflammatory markers and could be useful in the diagnosis of pancreatitis (4-7). Lipase/amylase ratio was hypothesized to differentiate the alcoholic pancreatitis and biliary pancreatitis. However this differentiation is important to make a definitive decision whether the patient with elevated serum amylase and lipase levels are caused by pancreatitis or not and more important for the best patient evaluation.

As radiologic imaging method, ultrasonography (US) is a valuable tool but contrasted abdominal tomography gives more detailed information. Balthazar score is the pancreatitis severity classification system based on the abdominal computed tomography (CT) (8-10). Besides, magnetic resonance imaging (MRI) can be used in the diagnosis especially for specific populations that CT could not be used and/or contraindicated. Unfortunately radiologic imaging with US is examiner dependent and CT or MRI is not available in all healthcare settings. So, laboratory results such as elevated amylase and lipase levels are still important in the diagnosis.

In this study we aimed to assess the value of the lipase/amylase ratio and MPV in the prediction of severity in adult ICU patients with pancreatitis. The importance of this study is the evaluation of the patient group with high amylase and lipase levels (higher than 3 times from upper limits for both markers), hospitalized with pre-diagnosis of acute pancreatitis but not have pancreatitis in the CT as the gold standard test.

MATERIALS AND METHODS

This is a retrospective observational study. Study protocol was approved by local ethical committee and all procedures performed according to Helsinki declaration. The study is on hospital-based Turkish population.

All adult patients hospitalized in a tertiary-care setting with the diagnosis of non-traumatic pancreatitis between January 1st, 2010 and December 31st, 2015have been analyzed retrospectively. Demographics (age, sex, diagnosis, hospitalization time, and prognosis), laboratory results and Ranson scores were recorded from hospital records in admission and after 48 hours.

Blood samples were collected and analyzed according to standard hospital procedures CELL-DYN Ruby (Abbott, USA) hematology device was used to analyze the hematology parameters. A Cobas® 6000 analyzer (Roche Diagnostics, USA) device was used to analyze the biochemical markers including amylase and lipase. All devices used in the analyses were located in the core laboratory. All devices are being calibrated regularly by accredited staff. Lipase/amylase ratio was calculated by dividing lipase result to amylase result for all subjects.

A 4-MDCT scanner (Siemens Healthcare, Germany) was used to examine the CT scans and all the procedures were performed according to referring hospital's routine procedures. The first available contrast-enhanced CT was re-assessed by primary radiologist on PACS (picture archiving and communication system) and Balthazar scores (between 0 and 10) were recorded. Patients were divided into two groups as group 1(subjects that having a Balthazar score of 0) according to CT reports. Group 2 were subjects having Balthazar score between 1 and 3.

No selection criteria were applied and all patients were enrolled consecutively. Patients without sufficient data and under 18 years old were excluded from the study.
Statistical analyses Descriptive statistics were stated as frequency, percentage (%) and mean ± standard deviation (SD). Kolmogorov-Smirnov test was used to

assess the normal distribution of the data. Differences between laboratory measurements were compared with Student's t-test. For comparison of categorical data Chi-square test was used. Wilcoxon test was used to compare two paired groups' data. One-Way-ANOVA test was used to compare means of three or more samples. All statistical tests were performed with the Predictive Analytics Software (PASW®, version 18, SPSS Inc., Chicago, IL).

RESULTS

A total of 528 patients were screened retrospectively and 398 patients were included in the study. There was not any CT imaging available for 102 patients, 19 patients were excluded for having insufficient recorded data, and 9 of them had a Balthazar score greater than 3. Mean age was 58.87±18.65 and 245 (61.6 %) of the subjects were female. Death occurred in 3 (0.8 %) patients. According to Balthazar scoring system, CT severity index (CTSI) was recorded as follows:1 for 119 (29.9%) patients, 2 for 65 (16.3%) patients, and 3 for 82 (20.6%) patients. A total of 132 (33.4 %) patients were classified as level 0, meaning that they had radiological normal pancreas. Among group 2, 217 (81.6%) patients had a biliary stone as underlying cause and 49 (18.4%) of them were non-biliary group. Laboratory results were given in table 1.

For the assessment of initial values, while amylase, glucose, urea, creatinine, C-reactive protein (CRP), hemoglobin (Hgb), hematocrit (Htc), WBC levels were significantly different between pancreatitis and non-pancreatitis groups according to CT imaging; lipase, age, Ranson score, alanine amino transferase (ALT), calcium (Ca), sodium (Na), potassium (K), mean platelet volume (MPV), and platelets count (Plt) levels did not show any difference. According to ROC analyses, area under the curve (AUC) levels were 0.636 (amylase), 0.559 (lipase), and 0.623 (WBC) (Figure 1). Additionally, there was not any correlation between amylase (p=0.803) and lipase (p=0.387) levels for the Balthazar score. After 48 hours, all parameters improved significantly, but sodium, hemoglobin, and MPV levels did not show any significant change.

Our results showed that mean amylase and lipase levels were high for both group 2 (1779.44±1214.46; 1932.68±1642.06, respectively) and group 1 (1320.55±1252.24; 1719.81±1501.60, respectively). To assess if there was any additional finding to distinguish higher Balthazar score subjects from high amylase and high lipase patients, we performed a subgroup analysis according to lipase/amylase ratio of 1. Chi-square analysis showed a significant difference for lipase/amylase ratio of 1 and pancreatitis (p=0.006) (Table2). The sensitivity and specificity to predict the severity of pancreatitis with lipase / amylase ratio at >1.0 was 50 % and 67 %, respectively.

According to subgroup analysis among group 2 (n=266) amylase, lipase, glucose, and ALT levels were different between biliary (n=217) and non-biliary (n=49) pancreatitis groups; but age, Ranson score, urea, creatinine, Ca, Na, K, CRP, Hgb, Htc, WBC, MPV, and Plt levels were not different between two groups.

DISCUSSION

Our study showed that lipase/amylase ratio can be a useful parameter to predict the severity of pancreatitis patients which have elevated amylase and lipase levels and hospitalized in adult ICU. However, MPV does not seem to be used effectively for the prediction of the severity of pancreatitis.

Female subjects were higher in both groups and that was compatible with literature (11). Mean age and hospitalization time for pancreatitis group was also compatible with literature (1, 11). Death ratio in our study group (0.7%) was lower than literature (4-6%) (8,12).

The serum amylase has been used as the essential laboratory test in the diagnosis of acute pancreatitis but there are limitations to use amylase alone in determining the presence of acute pancreatitis. Serum lipase is also a widely accepted marker for the diagnosis of pancreatitis and derived mainly from pancreatic acinar cells. The sensitivity and specificity of amylase and lipase is limited in many clinical conditions such as hypertriglyceridemia, intraabdominal inflammatory events, parotid and submandibular pathologies, renal insufficiency.

Table 1. Laboratory results of the groups.

	Balthazar score of 0 (Group 1)	Balthazar score between 1-3 (Group 2)	Total	p*	95% CI	p** 95% CI
Gender (Female/Male)	72/60	173/93	245/153	0.049***	NA	NA
Age	60.47±19.06	58.08±18.42	58.87±18.65	0.384	NA	NA
Hospitalization time (day)	5.53±3.86	6.44±8.14	6.14±7.03	0.222	-2.39-0.56	NA
Amylase	1320.55±1252.24	1779.81±1501.59	1627.25±1244.49	0.000	(-715.73)– (-202.05)	NA
Lipase	1719.81±1501.59	1932.68±1642.06	1862.08±1598.11	0.211	-547.13 / 121.39	NA
Ranson H0	1.41±0.94	1.27±0.87	1.32±0.89	0.484***	NA	0.000****
Ranson H48	0.69±0.74	0.67±0.81	0.67±0.78	0.583***	NA	
Glucose H0	115.03±44.80	126.83±55.46	123.04±52.51	0.041	-23.10-0.51	0.000 8.55-22.45
Glocose H48	114.26±40.32	111.40±40.25	112.24±40.23	0.576	-7.18-12.89	
Urea H0	42.77±35.00	36.28±21.15	38.44±26.71	0.023	0.90-12.08	0.000 3.81-7.71
Urea H48	37.58±30.24	30.66±19.52	32.80±23.54	0.014	1.42-12.43	
Creatinine H0	1.04±0.89	0.83±0.41	0.89±0.62	0.001	0.09-0.34	0.004 0.02-0.09
Creatinine 48	0.96±0.69	0.76±0.39	0.82±0.51	0.001	0.08-0.31	
ALT H0	170.57±286.92	164.41±161.27	166.46±211.25	0.786	-38.34-50.65	0.000 58.98-86.16
ALT H48	103.02±190.19	90.88±91.63	94.69±130.64	0.436	-18.45-42.73	
Calcium H0	8.67±0.90	8.69±0.69	8.68±0.77	0.847	-0.18-0.15	0.000 0.09-0.26
Calcium H48	8.49±0.72	8.49±0.69	8.49±0.70	0.983	-0.17-0.16	
Sodium H0	139.42±4.02	139.54±3.82	139.50±3.88	0.776	-0.94-0.70	0.270 -0.20-0.72
Sodium H48	139.89±3.12	139.36±3.29	139.53±3.24	0.173	-0.23-1.29	
Potassium H0	4.07±0.62	4.13±0.53	4.11±0.57	0.328	-0.18-0.06	0.000 0.08-0.24
Potassium H48	4.05±0.59	3.99±0.56	4.01±0.57	0.390	-0.08-0.19	
CRP H0	61.21±74.88	94.03±95.48	83.22±90.44	0.001	-52.81- (-12.83)	0.000 -46.91- (22.79)
CRP H48	92.08±95.21	123.26±100.78	113.41±99.96	0.011	-55.10-(-7.24)	
Hemoglobine H0	11.98±2.04	12.54±2.04	12.36±2.05	0.011	-0.99-(-0.13)	0.265 -0.34-1.22
Hemoglobine H48	11.16±1.83	12.13±5.68	11.83±4.84	0.097	-2.11-0.18	
Hematocrite H0	36.29±5.25	38.18±5.79	37.55±5.68	0.002	-3.08-(-0.69)	0.000 1.71-2.75
Hematocrite H48	34.17±4.98	36.11±5.09	35.51±5.14	0.002	-3.14-(-0.74)	
White blood cell H0	9.98±4.69	11.80±5.16	11.19±5.08	0.001	-2.88-(-0.76)	0.000 1.52-2.53
White Blood Cell H48	8.71±4.50	10.13±4.69	9.69±4.68	0.012	-2.52-(-0.32)	
MPV H0	9.24±1.78	8.93±1.67	9.03±1.71	0.101	-0.05-0.67	0.452 -0.24-0.11
MPV H48	9.09±1.78	8.94±1.61	8.99±1.66	0.451	-0.24-0.55	
Platelets H0	226.69±86.98	239.38±91.19	235.17±89.91	0.190	-31.71-6.33	0.000 11.52-23.52
Platelets H48	214.75±82.77	222.76±88.57	220.28±86.76	0.444	-2 8.58-12.56	

*: Independent Samples t-test , **: Paired Sample t-test, *** Chi-square test, ****Wilcoxon test, CI: Confidence Interval.
Reference values for the parameters: Amylase: 28-100 U/L, Lipase: 13-60 U/L, Glucose: 74-106 mg/dL, Urea: 13-43 mg/dL, Creatinine: 0.5-0.9 mg/dL, ALT: 5-33 U/L, CRP: 0-5 mg/L, Calcium: 8.4-10.4 mg/dL, Sodium: 136-145 mmol/L, Potassium: 3.5-5.1 mmol/L, Hematocrit: 34.8- 45 RU, White blood cell count: 3.9-11.7x103/mm3, Mean platelet volüme: 7.2-11.1 fL, Platelet count: 130-400x103/mm3)

However we can increase specificity of serum amylase levels by using a higher cutoff (3 times more than upper limit) and serum amylase levels does not correlate with etiology or severity (3, 13). It has been reported that serum lipase is more specific for alcoholic acute pancreatitis because most people with acute pancreatitis will have an elevated amylase, the benefit of adding a serum lipase test in the management of patients with acute pancreatitis is not clear (14). In our study, our subjects had high amylase and lipase levels (3 times more than upper level) too, and 132 of 398 (33%) subjects had a Balthazar score of 0. That may show that none of these markers are efficient in the diagnosis.

Amylase and lipase were studied as a marker of the severity of pancreatitis but no correlation was reported (15, 16). Gomez et al. suggested to use lipase alone rather than using with amylase to reduce costs, but amylase is still a very widely accepted marker in the diagnosis of pancreatitis (17, 18). Lipase/amylase ratio was suggested to differentiate alcoholic pancreatitis from biliary pancreatitis (6). Devanath et al. reported that a lipase/amylase ratio of 3 can be useful to differentiate alcoholic pancreatitis from other etiologies but not useful in prediction of severity (7). Tenner et al. reported a specificity of 100% and sensitivity of 31% for the serum lipase/amylase ratio greater than 5 (19). However, in their retrospective analysis of 56 patients (36 of them had alcoholic pancreatitis), King et al. reported that lipase/amylase is not sufficient to distinguish alcoholic from non-alcoholic acute pancreatitis (20). Our results suggested that, elevated lipase/amylase ratio (≥1) may predict the severity of ICU patients with pancreatitis.

Beyazit et al. reported that decreased MPV levels are decreased in acute pancreatitis (8.06±0.71 fL vs. 8.63±0.62 fL) and may provide additional information about severity (4). Additionally, Okuturlar et al. reported that MPV was higher in biliary pancreatitis than non-biliary pancreatitis (8.42±1.04 vs. 8.07±1.02) and could be an indicator of infection in early phases (14). Our results showed that there was no difference for MPV between higher and lower Balthazar score groups. That can be a result of the difference between study methods. Because, in referenced studies acute pancreatitis diagnosis was based on the presence of severe abdominal pain, vomiting, epigastric tenderness, and high serum amylase levels. However, in our study, severity classification was based on CT evaluation as gold standard in addition to clinical signs and high serum amylase and lipase levels.

Table 2. Crosstab of lipase:amylase ratio for the differential of pancreatitis and non-pancreatitis patients.

	Severity of Pancreatitis	
	Balthazar score 0	Balthazar score 1-3
L/A ratio <1	30	110
L/A ratio ≥1	62	112
Sensitivity = 112/222=50%; specificity =62/92=67%		

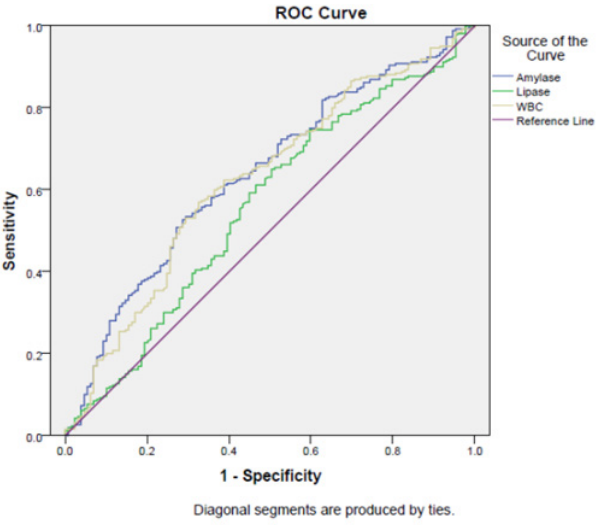

Figure 1. ROC curves for amylase, lipase, and WBC levels for the severity of pancreatitis.

CONCLUSION

Our findings suggested that lipase/amylase ratio can be beneficial to predict the severity of acute pancreatitis in adult ICU patients. However, MPV did not seem to be a good marker to predict the severity of pancreatitis. Further studies for specific patient groups such as pediatric and high CTSI patients can be beneficial.

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