Clinical and Experimental Health Sciences

Original Article / *Özgün Araştırma*

# *Serum Amylase Levels Can Predict Hospitalization and Operation Rates*

## Serum Amilaz Aktivitesi, Hastaneye Yatış ve Operasyon Oranlarını Öngörebilir

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## Abstract

**Objective**: The levels of serum amylase is an indicator of several diseases. Therefore, a routine amylase test is frequently requested in hospital emergency admissions. This research aims to evaluate the hospitalization and surgery rates of patients with high amylase levels.

**Methods:** A retrospective clinical study was performed on 64,909 patients aged 53.30±19.45 years who had a serum amylase test at hospital admission in the emergency ward between 2011 and 2015. Age, gender, serum amylase levels, diagnosis, hospitalization, and surgery status of the patients were obtained from the electronic medical records. The diseases were classified into seven groups according to the International Statistical Classification of Diseases and Related Health Problems codes. The patients were divided into three groups with respect to amylase levels– group 1 (<125 U/L), group 2 (125–375 U/L), and group 3 (>376 U/L). The results were statistically analyzed using the SPSS commercial tool package version 21.0. The $\chi 2$ test and Fisher's exact probability test were adapted for categorical variables, while Student's t-test was performed for the unpaired data of continuous variables.

**Results:** The hospitalization rate increased 2.4-fold and 4.7-fold and the surgery rate increased 1.6-fold and 1.4-fold in group 2 and group 3 compared to group 1, respectively. The hospitalization rate of the patients (N=571) in group 3 was 59.4%. Among them, only 93 patients were diagnosed with acute pancreatitis.

**Conclusion:** Elevated serum amylase levels can predict hospitalization and surgery status.

**Keywords:** Amylase, medical hospitalization, general surgery, hospital admission test

## Öz

**Amaç:** Serum amilaz düzeyi birçok hastalığın göstergesidir. Bu yüzden, rutin amilaz testi hastaneye acil başvurularda sıklıkla istenmektedir. Bu araştırmanın amacı, yüksek amilaz düzeyine sahip hastalarda hastaneye yatış durumu ve cerrahi riskleri değerlendirmektir.

**Yöntemler:** Acil serviste serum amilaz testi yapılmış, 53,30±19,45 yaşında 64909 hasta ile retrospektif klinik çalışma yapıldı. Yaş, cinsiyet, serum amilaz miktarı düzeyi, tanı, hastaların hastaneye yatış ve operasyonel durumlarına ait bilgiler tıbbi kayıtlar (Probel, Hastane İşletim Sistemi) kullanılarak elde edildi. Hastalıklar, ICD 10 kodlarına göre yedi grupta sınıflandırıldı. Serum amilaz düzeyleri amilaz konsantrasyonlarına göre üç gruba ayrıldı; Grup 1 (< 125 U/L), Grup 2 (125-375 U/L) and Grup 3 (> 376 U/L). Sonuçlar istatistiksel olarak SPSS ticari paket programı (versiyon 21,0) kullanılarak analiz edildi. Kategorik değişkenler için $\chi 2$ ve Fisher kesin olasılık testi; sürekli değişkenlerin eşleştirilmemiş verileri için ise Student t testi kullanıldı.

**Bulgular:** Hastaneye yatış ve ameliyat oranlarının Grup 2 ve Grup 3'te Grup 1'e göre sırasıyla 2,4 ve 4,7 ve 1,6 ve 1,4 arttığı saptandı. Amilaz değeri 376 U/L üzerinde olan hastaların (N=571) hastaneye yatış oranları %59,4 idi. Bu hastalardan yalnızca 93'ünde akut pankreas iltihabı vardı.

**Sonuç:** Yüksek serum amilaz düzeyi hastaneye yatış ve ameliyatı öngörmede kullanılan parametrelerden biri olabilir.

**Anahtar kelimeler:** Amilaz, hastaneye yatış, genel cerrahi, hastaneye kabul test

### INTRODUCTION

Serum amylase is influenced by many factors under both physiological and pathological conditions. Dysfunction of the amylase-producing glands might alter enzymatic activities, which can be important in different clinical conditions (1, 2). Indeed, serum amylase is a frequently requested test in patients presenting with acute abdominal pain in emergency wards (3, 4). Therefore, the serum amylase level is the most widely used biochemical marker in the diagnosis of many diseases. High serum amylase is detected in several diseases such as acute pancreatitis, pancreatic cancer, ectopic amylase-producing tumors, abdominal trauma, kidney dysfunction, severe burns, hyperlipidemia, and diabetic ketoacidosis (5-8).

Although there is a debate over the use of amylase alone, lipase alone, or amylase and lipase together to predict pancreatic diseases, there is a common tendency to perform at least one if not both of the tests in the emergency ward (3, 9-11). Current practice in our hospital is to perform amylase tests on all patients admitted to the emergency ward for diagnosis of acute pancreatitis. However, amylase could be useful for other diagnostic purposes.

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The aim of this study was to assess the hospitalization and surgery rates depending on serum amylase levels of patients at hospital admission in emergency service, not just for pancreatic disease.

## METHODS

### Study Design and Samples

This retrospective clinical study included 64,989 patients who were admitted to our hospital's emergency ward between January 2011 and January 2012. Patients lacking a serum amylase test were not included to the analysis, and data analysis was thus performed on 64,909 patients. Age, gender, serum amylase level, prediagnosis, hospitalization, and surgery status of the patients were obtained retrospectively from the laboratory information system. We enrolled all patients with available amylase levels in the database at the time of hospital admission at the emergency ward. The amylase levels in patients with different diagnoses were classified according to the International Statistical Classification of Diseases And Related Health Problems codes (ICD 10 Codes). The diseases associated with amylase levels in the literature were categorized into seven groups as K85 (acute pancreatitis), R10 (abdominal and pelvic pain), 81 (cholecystitis), E78 (lipoprotein metabolism disorders and other lipidemias), F32 (depressive episodes), F41 (anxiety disorders), and others (the rest of the diseases). It is well known that serum amylase includes 60% saliva amylase (1), so we included the diseases such as E78, F32, and F41, which in turn resulted in increased saliva levels in our study. Missing values for serum amylase were ignored.

This study involved retrospective data extracted from our laboratory information system (LIS-Probel, Hospital Operating System) and did not include any medical or healthcare interventions. Therefore, informed patient's consent was unexpected. This study was approved by the ethics and research committee of İstanbul Medipol University, in accordance with the Declaration of Helsinki.

### Laboratory Analysis

Amylase level (U/L) measurement based on the colorimetric test principle was performed with an autoanalyzer (Olympus AU640, Olympus Corporation, Japan). It is well known that serum amylase levels increase within hours of pancreatic injury, and a threshold amylase level three times the upper limit of normal (375 U/L) is recommended for diagnosis of acute pancreatitis (10, 12). Therefore, in our study patients were divided into three groups according to their amylase levels to determine whether high serum amylase level can predict the hospitalization and surgery rates. Group 1 had normal values (<125 U/L), group 2 had three times the normal level (125–375 U/L), and group 3 had over the three times the normal level (>376 U/L) (10).

### Statistical Analysis

The $\chi^2$ test and Fisher's exact probability test were performed for categorical variables, and Student's *t*-test for unpaired data of continuous variables was performed to compare clinicopathological characteristics between groups. Multivariate stepwise logistic regression analysis was performed to identify the independent risk factors associated with inpatients and operated patients. The multivariate odds ratios (ORs) are presented with 95% confidence intervals (CIs). Significant differences in serum amylase level between groups were determined using Bonferroni's post hoc test. In all of these analyses, data are presented as means±standard deviations or as numbers and percentages. A p-value <0.001 was considered statistically significant. All statistical calculations were carried out with Statistical Package for the Social Sciences version 21.0 (SPSS IBM Corp.; Armonk, NY, USA).

## RESULTS

### Demographic and Clinical Characteristics

The patients with recorded age, gender, amylase levels, and diagnosis (N=64.909) were included in the present study, and demographic and clinical characteristics are given in Table 1. The study included 29,080 (44.8%) men and 35,829 (55.2%) women aged 53.30±19.45 years (range 18–70 years). The patients were prediagnosed at hospital admission. Among all patients, 75% were outpatients and 25% were inpatients. Only 9.6% of the patients had an operation.

The data were divided into three groups according to the amylase levels of patients. The age distribution according to the different patient groups is shown in Table 2. The mean age of the patients was higher in groups 2 and 3 than the patients with normal amylase levels (group 1). There was a statistically significant difference between the amylase levels and the age of patients by ANOVA (p<0.001), and Bonferroni's correction for multiple comparisons showed a significant difference between the two age groups in groups 1 and 2 (p<0.001); groups 1 and 3 (p<0.001); and groups 2 and 3 (p<0.012). The numbers and percentages of patients categorized by amylase levels and diseases are shown in Table 3.

### Comparison between Inpatient and Outpatient Groups

Data for inpatient and outpatient groups classified by serum amylase levels are summarized in Table 4. In total, the percentages of outpatients and inpatients in groups 1, 2, and 3 were 76.7% and 23.3%; 55.4% and 44.6%; and 40.6% and 59.4%, respectively.

### Comparison between Operated and Non-operated Groups

Among all patients (N=64.909), the total number of operated patients was 6.225 (9.6%) (Table 5). The percentage of operated

**Table 1.** Characteristics of 64.909 patients admitted to the emergency ward

| | n | % |
|---|---|---|
| Total patients | 64.909 | 100.0 |
| Female | 35.829 | 55.2 |
| Male | 29.080 | 44.8 |
| Outpatient | 48.655 | 75.0 |
| Inpatient | 16.254 | 25.0 |
| Non-operated patients | 58.684 | 90.4 |
| Operated patients | 6.225 | 9.6 |

**Table 2.** Age distributions according to the patient groups

| Group | Amylase levels (U/L) | n (%) | Age (Mean±SD) |
|---|---|---|---|
| Group 1 | <125 | 60.331 (92.9) | 52.97±19.45 |
| Group 2 | 126–375 | 3.616 (5.6) | 60.79±17.94 |
| Group 3 | >375 | 962 (1.5) | 58.77±18.41 |
| Total | 64.909 (100.00) | | |
| U/L: units per liter; n: number of cases; SD: standard deviation | | | |

**Table 3.** Amylase levels in diseases diagnosed according to the ICD 10 codes Patients

| ICD 10 Codes‡ | Patients n (%) | Amylase levels (U/L) n (%) | Group 1 (<125 U/L) n (%) | Group 2 (125–375 U/L) n (%) | Group 3 (>376 U/L) n (%) |
|---|---|---|---|---|---|
| All patients | 64.909 (100.0) | 60.331 (92.9) | 3.616 (5.6) | 962 (1.5) | < 0.001 |
| R10 | 10.420 (16.0) | 9.422 (90.4) | 625 (6.0) | 373 (3.6) | |
| E78 | 415 (0.6) | 396 (95.4) | 19 (4.6) | 0 | |
| K85 | 623 (1.0) | 313 (50.2) | 144 (23.1) | 166 (26.6) | |
| F32 | 305 (0.5) | 277 (90.8) | 28 (9.2) | 0 | |
| K81 | 1.756 (2.7) | 1.547 (88.1) | 144 (8.2) | 65 (3.7) | |
| F41 | 282 (0.4) | 274 (97.2) | 8 (2.8) | 0 | |
| Others | 51.108 (78.8) | 48.102 (94.1) | 2.648 (5.2) | 358 (0.7) | |

‡ ICD 10 codes: R10-Abdominal and pelvic pain, E78-Lipoprotein metabolism disorders and other lipidemias, K85-Acute pancreatitis, F32-Depressive episodes, K81-Cholecystitis, F41-Anxiety disorders

U/L: units per liter; n: number of cases‡

**Table 4.** The number and percentages of outpatients and inpatients classified by serum amylase levels

| | Amylase levels (U/L) | | | | | |
|---|---|---|---|---|---|---|
| | Group 1 (<125 U/L) | | Group 2 (125–375 U/L) | | Group 3 (>376 U/L) | |
| ICD 10 Codes‡ | Outpatient n (%) | Inpatient n (%) | Outpatient n (%) | Inpatient n (%) | Outpatient n (%) | Inpatient n (%) |
| All patients | 46.262 (76.7) | 14.069 (23.3) | 2.002 (55.4) | 1.614 (44.6) | 391 (40.6) | 571 (59.4) |
| R10 | 7.499 (79.6) | 1.923 (20.4) | 273 (43.7) | 352 (56.3) | 165 (44.2) | 208 (55.8) |
| E78 | 392 (99.0) | 4 (1.0) | 18 (94.7) | 1 (5.3) | 0 | 0 |
| K85 | 102 (32.6) | 211 (67.4) | 45 (31.3) | 99 (68.8) | 73 (44.0) | 93 (56.0) |
| F32 | 158 (57.0) | 119 (43.0) | 2 (7.1) | 26 (92.9) | 0 | 0 |
| K81 | 937 (60.6) | 610 (39.4) | 75 (52.1) | 69 (47.9) | 31 (47.7) | 34 (52.3) |
| F41 | 242 (88.3) | 32 (11.7) | 7 (97.5) | 1 (12.5) | 0 | 0 |
| Others | 36.942 (76.8) | 11.160 (23.2) | 1.582 (59.7) | 1.066 (40.3) | 122 (34.1) | 236 (65.9) |

‡ ICD 10 codes: R10-Abdominal and pelvic pain, E78-Lipoprotein metabolism disorders and other lipidemias, K85-Acute pancreatitis, F32-Depressive episodes, K81-Cholecystitis, F41-Anxiety disorders

U/L: units per liter; n: number of cases

**Table 5.** The numbers and percentages of operated and non-operated patients classified by amylase levels

| | Amylase levels (U/L) | | | | | |
|---|---|---|---|---|---|---|
| | Group 1 (<125 U/L) | | Group 2 (125–375 U/L) | | Group 3 (>376 U/L) | |
| ICD 10 Codes ‡ | Non-operated n (%) | Operated n (%) | Non-operated n (%) | Operated n (%) | Non-operated n (%) | Operated n (%) |
| All patients | 54753 (90.8) | 5578 (9.2) | 3088 (85.4) | 528 (14.6) | 843 (87.6) | 119 (12.4) |
| R10 | 8685 (92.2) | 737 (7.8) | 518 (82.9) | 107 (17.1) | 345 (92.5) | 28 (7.5) |
| E78 | 396 (100) | 0 | 19 (100) | 0 | 0 | 0 |
| K85 | 272 (86.9) | 41 (13.1) | 133 (92.4) | 11 (7.6) | 154 (92.8) | 12 (7.2) |
| F32 | 271 (97.8) | 6 (2.2) | 16 (57.1) | 12 (42.9) | 0 | 0 |
| K81 | 1260 (81.4) | 287 (18.6) | 120 (83.3) | 24 (16.7) | 53 (81.5) | 12 (18.5) |
| F41 | 269 (98.2) | 5 (1.8) | 8 (100) | 0 | 0 | 0 |
| Others | 43600 (90.6) | 4502 (9.4) | 2274 (85.9) | 374 (14.1) | 291 (81.3) | 67 (18.7) |

‡ ICD 10 codes: R10-Abdominal and pelvic pain, E78-Lipoprotein metabolism disorders and other lipidemias, K85-Acute pancreatitis, F32-Depressive episodes, K81-Cholecystitis, F41-Anxiety disorders

U/L: units per liter; n: number of cases

**Table 6.** Results of multivariable logistic regression; risk factors for hospitalization and operation rates

| | Hospitalization | | | Operation | | |
|---|---|---|---|---|---|---|
| **Covariate** | **OR** | **95% CI** | **p** | **OR** | **95% CI** | **p** |
| Gender | | | | | | |
| Male vs. female | 1.597 | 1.540–1.656 | <0.001 | 1.731 | 1.642–1.826 | <0.001 |
| Age (Years) | | | | | | |
| <50 vs. 50+ | 1.012 | 1.011–1.013 | <0.001 | 1.003 | 1.002–1.004 | <0.001 |
| Amylase Levels (U/L) | | | | | | |
| ≤125 vs. 126–375 | 2.399 | 2.182–2.507 | <0.001 | 1.550 | 1.406–1.708 | <0.001 |
| ≤125 vs. ≥376 | 4.658 | 4.084–5.313 | <0.001 | 1.373 | 1.130–1.669 | <0.001 |
| OR: odds ratio; CI: confidence interval | | | | | | |

patients with normal amylase level was 9.2%. However, the percentages rose to 14.6% and 12.4% for group 2 and group 3, respectively.

**Relation of Serum Amylase Levels to Hospitalization and Surgery**

The hospitalization rates for the groups based on amylase levels were 23.3% for group 1, 44.6% for group 2, and 59.4% for group 3 (Table 4). The results of multivariable logistic regression to evaluate risk factors for hospitalization rate are shown in Table 6. The difference between the hospitalization rates of the groups based on amylase levels was statistically significant (p<0.001). The hospitalization rate was associated with gender, age, and serum amylase levels. The differences in gender, age, and serum amylase levels between outpatients and inpatients were compared with a $\chi^2$ test, and they were found to be statistically significant (p<0.001). Furthermore, multivariable logistic regression analysis revealed the risk factors for hospitalization. According to this analysis, being male [p<0.001, OR=1.597 (95% CI: 1.540–1.656)], being over the age of 50 [p<0.001, OR=1.012 (95% CI: 1.011–1.013)], having amylase levels of 126–375 U/L (group 2) [p<0.001, OR=2.399 (95%CI: 2.182–2.507)], and having amylase levels over 376 U/L (group 3) [p<0.001, OR=4.658 (95% CI: 4.084–5.313)] were independent risk factors.

The results of the multivariable logistic regression to evaluate risk factors for operation rate are shown in Table 6. The risk factors for undergoing surgery included being male [p<0.001, OR=1.731 (95%CI: 1.642–1.826)], being over the age of 50 [p<0.001, OR=10.45 (95%CI: 1.050–104.1)], having amylase levels of 126–375 U/L (group 2) [p<0.001, OR=10.45 (95%CI: 1.050–104.1)], and having amylase levels over 376 U/L (group 3) [p<0.001, OR=10.45 (95%CI: 1.050–104.1)].

## DISCUSSION

Hyperamylasemia is a common result of pancreatitis but can also be a reflection of non-pancreatic disease (12). Elevation of serum amylase is observed in 14%–80% of critically ill intensive care unit patients who do not have prior pancreatic disease. Elevated amylase levels represent a pancreatic manifestation of multisystem organ failure, inflammation, and oxidative stress (13).

In a Scandinavian study, increased pancreatic enzyme level was noted in 8% of hospitalized patients with non-pancreatic diseases, but pancreatic abnormalities were only found in a few patients (14). Weaver et al. (15) observed in a study of 192 patients that 26% (n=18) of all hyperamylasemia patients (n=70) had an elevation of the pancreatic isoamylase fraction, and the remaining 74% (n=52) of the patients were hyperamylasemic due to elevations in the non-pancreatic isoamylase fraction or to both the pancreatic and non-pancreatic isoamylase fractions.

For decades, serum amylase levels have been determined in the emergency wards for the diagnosis of pancreatic diseases. Although medical records contain important clinical information, they might not be accepted as reliable sources for scientific research due to often the poor agreement between the patients and the professionals who record the data (16). Accordingly, we took the data from the electronic medical record system in order to minimize such errors. In this study, we obtained serum amylase level from 64.909 patients with different clinical diagnoses between the years 2011 and 2012 and compared the amylase levels with their hospitalization and surgery status. The reason for choosing this period was that in those years it was compulsory to require serum amylase levels tests upon hospital admission in an emergency ward. There are some studies that have reported that amylase levels more than three times the reference value support the diagnosis of acute pancreatitis (10, 17, 18). However, we found that high serum amylase levels (over 125 U/L) predicts hospitalization and surgery rates for both pancreatic diseases and other diseases. Likewise, Frulloni et al. (5) reported that several conditions other than pancreatitis can be the cause of elevated serum amylase and/or lipase levels in patients both with and without abdominal pain. We found that patients with hyperamylasemia regardless of the disease also had increased risks for hospitalization and for having surgery. In the group of "other diseases," the percentages of inpatients were increased with elevated serum amylase levels. Moreover, among all patients, the number of inpatients was increased with elevated serum amylase levels. At hospital admission, if the serum amylase level was 126–375 U/L, the risk for hospitalization increased 2.6-fold (OR 2.647), and if the value was over 376 U/L the risk increased 4.8 fold (OR 4.788).

Consistent with the literature (5, 19), the serum amylase levels of the patients with R10-abdominal pelvic pain (3.7%), K85-acute pancreatitis (26.6%), and K81-cholecystitis (3.7%) were higher than the mean amylase level (1.5%) of all patients over 360 U/L. There were no patients with anxiety disorders, depressive episodes, or hyperlipidemia in group 3, even though many studies have referred to high saliva

amylase level (20, 21). In all groups of diseases, the patients with abdominal and pelvic pain made up the highest percentage (16.0%). Although the patients with acute pancreatitis accounted for 0.96% of all patients, 26.6% of these patients had amylase level over 376 U/L.

Male patients and patients older than 50 years old were also considered at elevated risk for hospitalization and surgery. Previous studies indicated the relation between amylase level and age, and higher serum amylase levels were noted in subjects aged 55 years or more compared to younger subjects (22). Our results confirm a statistically significant correlation ($p<0.001$) between the serum amylase levels and the patients' ages. To date, no large scale epidemiological studies have been conducted to explore the association between high serum amylase levels and hospitalization and surgery rates.

In this study, the data for patients lacking serum amylase measurements were not included in the analysis. Despite this limitation, the large majority of the population in the present study was clearly well documented in terms of medical records that included age, gender, serum amylase level, diagnosis, hospitalization, and surgical status of the patients.

## CONCLUSION

In conclusion, our results suggest a robust association between high serum amylase level and hospitalization and surgery rates. Serum amylase levels were higher in the inpatients and the operated patients, indicating that the elevated serum amylase level might be a biomarker for predicting hospitalization and surgery.

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**Ethics Committee Approval:** Ethics committee approval was received for this study from the ethics committee of İstanbul Medipol University (Ethical approval number/date: 10840098-604.01.01-E.2226 / 16.09.2015).

**Informed Consent:** In this study retrospective data extracted from hospital laboratory information system (LIS-Probel, Hospital Operating System) was collected and analysed, therefore informed consent was unexpected.

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