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CAN SERUM AMYLASE LEVEL EVALUATION FACILITATE EARLY DIAGNOSIS OF ACUTE APPENDICITIS, AS AN ADJUNCTIVE BIOMARKER?

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ABSTRACT

Introduction: *Acute Appendicitis is considered as a medical emergency, one of the most prevalent etiologies for acute abdominal pain. Perforated cases of acute appendicitis are possible sequences of late diagnosis. One of the biomarkers that can be a potential target in diagnosis of acute appendicitis is serum amylase level evaluation which this study is focused on.*

Material and Method: *627 patients with acute abdominal pain included in the trial. 125 cases out of these 627,18-65 years old patients with acute abdominal pain whom were suspected of appendicitis were undergone appendectomy surgery due to clinical and paraclinical scoring during standard treatment. At arrival serum amylase evaluation was done for all participants. Macroscopic reports of surgery and histopathologic reports have been recorded. Amylase serum level and its correlation with the acute appendicitis diagnosis and their complications were analyzed with the use of variance test, chi-square tests, ROC curve.*

Results: *Findings showed, in patients with normal appendix, serum amylase level mean was 55.40mg/dl, and in patient with simple acute appendicitis was 33.32mg/dl, and in complicated appendicitis was 62.40mg/dl which had statistically significant differences (P-value=0.003). Data also showed serum amylase level in the diagnosis of complicated appendicitis in the cutting point 34.5, had Sensitivity , specificity,positive predictive value,negative predictive value 100%, 56%, 64.5% and 100%, and the total accuracy of the test is 75.5%.*

Conclusion: *Serum amylase level can be used in more precise diagnosis of acute appendicitis, complicated appendicitis as an adjunctive biomarker. possibly it can help that acute appendicitis and its complication get early diagnosis.*

KEYWORDS: *Amylase, Acute Appendicitis, Early Diagnosis*

INTRODUCTION:

Acute Appendicitis is considered as a medical emergency and one of the most prevalent factors of causing simple acute abdominal pain in the whole world. In case of delayed treatment in acute appendicitis, inflammatory appendix tissue will be perforated and peritonitis and shock can be the sequences. This mechanism is rational of high mortality in such case. **[***Pruekprasert P et al., 2004***]** The symptoms of acute appendicitis can mimic symptoms of many abdominal illness such as gastritis, abdominal lymphadenitis, ovarian cysts in women, acute salpingitis, intestinal and parasitic infections, kidney stone, and urinary tract infections**. [***Wagner M et al., 2018***]**

Decision making about diagnosis of acute appendicitis is a difficult decision. scoring criteria

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such as Alvarado score and appendicitis inflammatory response score as a basis of patient history, physical examination and laboratory markers such as leukocytosis and CRP are used for the acute appendicitis diagnosis **[***Alvarado A,1986; Andersson M, Andersson RE, 2008; Kollár D et al., 2015; Andersson M et al., 2017; Salih IK et al., 2018***]**. Other diagnostic methods including abdominal sonography, CT scan and MRI have adjunctive role in confirmation of diagnosis. All these biomarkers diagnosis decrease of error rate. Nevertheless, the value of laboratory test are yet under discussion. **[***Horng-Ren Y et al., 2005***]**

Despite various study for improve the accuracy of acute appendicitis, 15 to 30 percent of normal appendix unnecessary surgery. **[***Salih IK et al., 2018***]** in this regard use of a sensitive, cheap, available para clinic biomarker can prevent unnecessary surgery and extra costs.

Amylase is considered as a hydrolyzing enzyme that breaks 1 and 4 alpha links and also polysaccharides such as glycogen and starch and changes it into maltose. Naturally amylase is secreted from pancreatic acinar cells and then duodenum and in intestine it changes starch into simpler sugars. If an inflammation is created in pancreas or salivary glands, more amount of amylase is released into blood **[***Matull W et al., 2006***]**. Also some studies revealed that serum amylase level may increase in other abdominal inflammations such as appendicitis. **[***Yadav D et al., 2002***]**

Because of high prevalence rate of acute appendicitis as an etiology for acute abdominal pain use of adjunctive lab tests in conjunction with clinical scoring methods can increase early diagnosis rate and can prevent possible complications and unnecessary surgeries. Amylase level evaluation ability for diagnosis of acute appendicitis is the aim of this study.

Material and methods:

In this study 627 patients with abdominal pain which has been initiated during last 6 hours included in the trial. The patients have been gone standard treatment for evaluation for acute abdomen. All standard measures and routine tests and treatment for patients were administered. 125 cases out of these 627,18-65 years old patients with acute abdominal pain whom were suspected of appendicitis were undergone appendectomy surgery due to clinical and paraclinical scoring during standard treatment. At arrival serum amylase evaluation was done for all participants. Blood sample was taken (2cc) from all patients and amylase biomarker level was measured by the way of sigma Maltotetroase demographic characteristics and clinical data and lab tests have been recorded. All Evaluations have been conducted by an Emergency Medicine Specialist. participants were checked for acute appendicitis diagnosis confirmation based on standards. The patient with underlying inflammatory disease and pregnancy were the exclusion criteria. Macroscopic reports of surgeon during operation, have been recorded. After then all tissue sample of patients who underwent appendectomy were sent to pathology laboratory of hospital for histopathology confirmation. The pathology report considered as gold standard for confirmed diagnosis of acute appendicitis. The data and variables of Amylase serum level and its correlation with the acute appendicitis diagnosis and their complications were analyzed with the use of variance test, chi-square tests, ROC curve. Data variables consist of quantitative for amylase serum level and qualitative variable for the identified diagnosis for patients, have been analyzed using analytic test. Obtained information from explanation of operation and laboratory and pathological results were collected and with the use of variance test, chi-square tests, ROC curve, the data were analyzed. Statistical measured results were reported in the form of mean, standard deviation, positive/negative predictive value, Sensitivity and specificity. And ROC curves were drawn. The software used in SPSS V-20, and significance level of tests were considered less than 5%. This project has been granted ethic`s code of IR.AJUMS.REC.1398.077 by Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran ethics committee..

To overcome it is possible, due to the uniting the knowledge and will of all doctors in the world

Results

The aim of this study was determination of efficacy of serum amy-

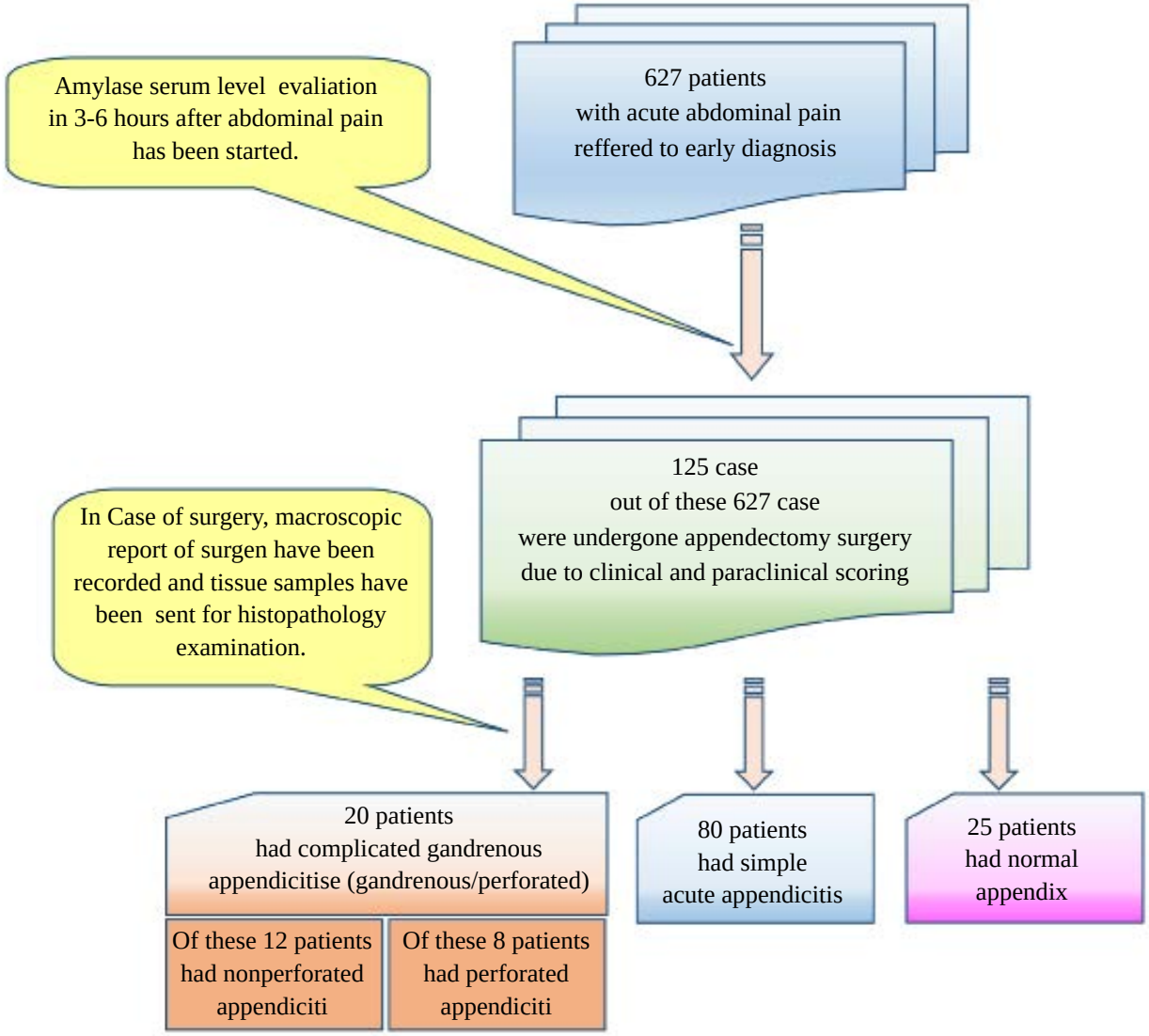

Figure1. *Study Design.*

Table 1.

The comparison of the serum amylase level in patients divided by the type of diagnosis

group	mean	SD	P-value[1]	Differences of mean	P_value[2]
Normal appendix, simple acute and complicated appendicitis					
Normal appendix (n=25)	33.32	16.25		-29.08	0.002
Simple acute appendicitis (n=80)	55.40	30.72	0.003	22..8	0.003
Complicated appendicitis (n=20)	62.40	44.90		7	0.372
Acute, normal and gangrenous perforated					
Normal appendix (n=25)	33.32	16.25		22.08	<0.001
Simple acute appendicitis (n=80)	55.40	30.72	0.001	28.60	0.6
Gangrenous perforated appendicitis(n=8)	84	65.98		50.68	0.188
Simple acute appendicitis, non-perforated gangrenous appendicitis and normal group					
Normal appendix (n=25)	33.32	16.25		14.68	0.123
Simple acute appendicitis (n=80)	55.40	30.72	0.002	22.08	0.001
Gangrenous non perforated appendicitis(n=12)	48	12.13		7.40	0.376

Notes: SD- Standard deviation, [1]Anova analysis (analysis of variance) ,[2]LSD analysis (Least Significant Difference)

lase level as a diagnostic criterion for simple acute appendicitis. From 125 patients with acute appendicitis which underwent surgery, 25 patients (20 %) had normal appendix diagnosis, 80 patients (64 %) had simple acute appendicitis and 20 patients (16 %) had complicated appendicitis (gangrenous / perforated). Among complicated cases, 8 out of 20 patients were complicated with perforated gangrenous appendicitis and 12 out of 20 patients were involved with non-perforated gangrenous appendicitis. (figure 1)

Our study results revealed that the mean of amylase serum level in patients with normal appendix (55.40mg/dl), simple acute appendicitis is (33.32mg/dl) and complicated appendicitis (gangrenous and perforated) (62.40mg/dl) had statistically significant differences. (P-value=0.003). Also in pairwise comparisons there was statistically significant differences between normal appendix with simple acute appendicitis (P value=0.003) and complicated appendicitis with normal group (P value=0.002). (table 1 and figure 2 Points A,B, and D)

Our study data demonestrated that the mean of amylase serum level in patients with normal appendix (55.40mg/dl), Simple acute appendicitis (33.32mg/dl) and gangrenous perforated appendicitis (84mg/dl) had statistically significant differences. (P-value=0.001). Also in pairwise comparisons there was no statistical difference between gangrenous perforated appendicitis with normal group (p value=0.188) and acute simple appendicitis with perforated gangrenous (p value=0.6). (table 1 and figure 2 Points A,B, and C)

Based on the results of our study, the mean of amylase serum level in three groups simple acute appendicitis, gangrenous appendicitis non-perforated, and normal appendix had statistically significant differences (P-value =0.002). but in pairwise comparisons between non-perforated gangrenous appendicitis with normal group(p value=0.123) and simple acute appendicitis with non-perforated gangrenous there was no statistical differences(p value=0.376). (table1 and figure 2 Points A,B, and E).

According to the ROC curve analysis, serum amylase level had Sensitivity, specificity, positive and negative predictive value 65%, 64%, 92.9% and 42.9% in simple acute appendicitis diagnosis.

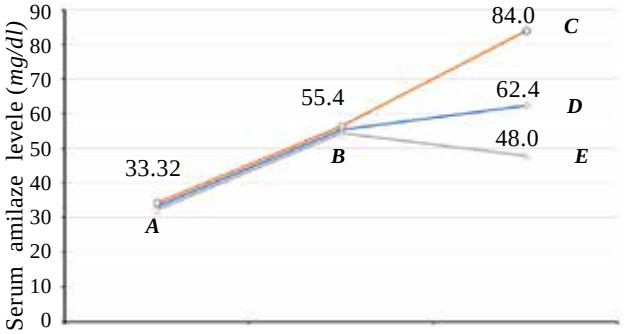

***Figure** 2: The mean level of serum amylase (normal group (A), simple acute appendicitis (B), perforated gangrenous appendicitis (C), complicated (D) and non-perforated gangrenous appendicitis(E))*

(P<0.05). Based on the ROC curve analysis of serum amylase level in diagnosis of complicated appendicitis it had Sensitivity, specificity, positive and negative predictive value of 100%, 565, 64.5% and 100%, respectively. (P=<0.05).(table 2 and figure 3

Discussion

Several studies have focused on the diagnostic value of the serum amylase level in diagnosis of acute appendicitis.

A case report study that Jon Won Um and colleagues have done in 1999, In this study a patient woman aged 17 years old one day before referring she had epigastric abdominal pain and Right Lower Quadrant pain. In this patient serum amylase level was high, but lipase was normal after appendectomy abdominal pain in patient gone decrease. Concluded, this study showed the serum amylase level increase in acute appendicitis [*Um JW et al., 1999*]. Similarly, our study confirmed serum amylase level increasing in acute-phase of appendicitis.

In a cross-sectional study that Amanollahzadeh and his colleagues have done over 61 children with acute phase appendicitis that underwent appendectomy. The result of this study showed serum amy-

Table 2.

Sensitivities, Specificities,PPV, NPV and Diagnostic Accuracy of serum amylase level

Goups	Sen (%)	Spe (%)	PPV (%)	NPV (%)	DA
Simple acute appendicitis	65	64	92.2	42.9	69.5
Complicated appendicitis	100	56	62.5	100	75.5
Notes: Sen - Sensitivity , Spe - Specificity, DA - Specificity, PPV - positive predictive value, NPV - negative predictive value					

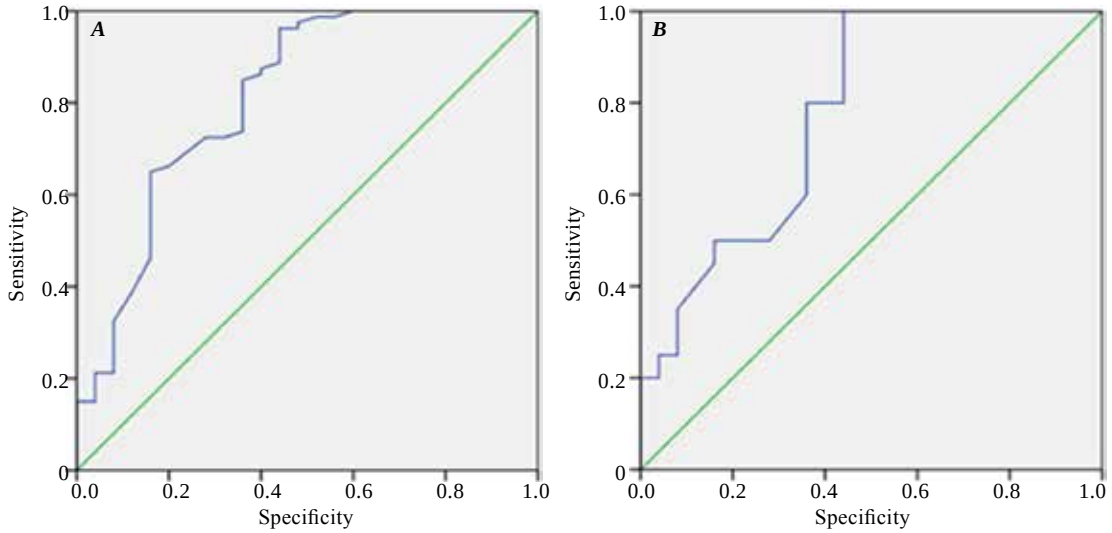

Figure3: *ROC curve of amylase serum level in simple acute appendicitis diagnosis (A) and of complicated appendicitis (B).*

lase level had sensitivity 89%, and Specificity 100% for perforated acute appendicitis [*Amanollahi O, Tat S, 2018*]. Although the children were not evaluated in our study and design of this study is not the same as our study, our findings revealed serum amylase level had sensitivity, specificity of 100% and 56% in diagnosis of acute appendicitis.

In 1981 Swensson EE and Maull KI have done a study as (clinical significance of serum and urine amylase level increase in patients with acute appendicitis) in which 251 patients with acute appendicitis were checked during a 45-month period, that in 155patients serum and urine amylase level were recorded before surgery. That showed serum amylase level increase in acute appendicitis. At the end the result showed that (1) acute appendicitis and the increase in amylase level may happen at the same time. (2) Hyperamylasemia and hyperamylasuria should not prevent the surgeon from initial operation, if the other clinical characteristics signify appendicitis surgery should be done and (3) abdominal pain and increase in amylase level show a significant disease in abdomen, not a disease in pancreas **[***Swensson EE, Maull KI, 1981***]**. The findings in the above-mentioned study concerning the increase in amylase level in patients with acute appendicitis are similar with findings of our study.

In a study that Jon Won Um and colleagues have done in 1999 stated that macro amylase is a continuous situation and an increasing serum amylase action that has not a clear clinical symptom in pancreatic disorder. In this study a patient woman aged 17 years old with macro amylase and acute appendicitis. One day before referring she had epigastric abdominal pain and Right Lower Quadrant pain. In this patient serum amylase level was high, but lipase was normal. The patient underwent appendectomy and the abdominal pain decreased. At the end the results showed that serum amylase level increase can be considered as a criterion for diagnosis of acute appendicitis **[***Um JW et al., 1999***]**. Even if in the above study only one case was introduced, but the obtained findings are totally favorable with our findings that serum amylase level increase in patients with acute appendicitis.

In a cross-sectional study that Amanollahzadeh and his colleagues have done over 61 children with diagnosis of acute appendicitis that underwent appendectomy. In a cross-sectional study between 2015-2016, 61 of 3-15 years old children were underwent appendectomy surgery due to acute appendicitis diagnosis. By checking histopathology the diagnosis of appendicitis was confirmed. Before surgery serum samples were taken and serum amylase, lipase, Alkane Phosphatase, Alanine amino transferase (ALT) and Aspartate Amino transferase (AST) were checked. Mean of (standard deviation) serum amylase level in perforated appendicitis group 69.2 (28.9) mg/dl and in non-perforated appendicitis group 29.9 mg/dl($p<0.001$). Serum amylase sensitivity 89%, and Specificity 100% were predicted for perforated acute appendi-

citis, in serum level of 46 mg/dl. They concluded that amylase serum level of perforated appendicitis patients in comparison to non-perforated appendicitis patients dramatically have increased. Serum amylase for prediction of perforated appendicitis is useful. **[***Amanollahi O, Tat S, 2018***]** This mentioned study also confirms our study data, although they evaluated the patients of pediatric age groups. Mean of serum amylase level between two groups of our study, normal appendix diagnosis with complicated appendicitis had statistically significant differences, (p-value =0.002).

Conclusion

In conclusion, the mean serum amylase level in complicated and simple acute appendicitis were higher than normal group. Serum amylase can possibly have high accuracy in the complicated appendicitis diagnosis.

Amylase serum level can be used in more precise diagnosis of acute appendicitis, complicated appendicitis as an adjunctive biomarker. Possibly it can help early diagnosis for acute appendicitis and its complication

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THE NEW ARMENIAN MEDICAL JOURNAL
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CONTENTS

THE NEW ARMENIAN MEDICAL JOURNAL

Vol.16 (2022). No 2

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