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Serum amylase level measurement in acute abdominal pain

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Abstract

Acute abdominal pain is a frequent symptom to the emergency department, can be caused by various pathologic processes. The aim of this study was to appraise the role of serum amylase level in diagnostic workup of non-traumatic adult patients presented with acute abdominal pain to surgical emergency department (ED).

Our study is based on data collected retrospectively from patients' medical records admitted to Shar Emergency Surgical Unit, Sulaimani, Iraq from 10th January 2019 to 20th May 2019. All non-traumatic adult patients with acute abdominal pain within twenty-four hours before admission were included and serum amylase levels were measured on admission using Enzyme-Linked Immunosorbent Assay (ELISA) available at (ED).

Overall, 68 patients were included, with mean age of 45.9 years over the aforementioned time period, 44 females (64.7%) and 24 males (35.3%), of which 37 patients had normal serum amylase level (14 male and 23 female patients), defined as levels between (35 IU/L-115 IU/L) by the laboratory (ELISA) device used for all the tests, while the other 31 patients (10 males and 21 females) had high serum amylase levels due to different disease processes, the most common two with equal frequencies were acute calculous cholecystitis (41.9%) and acute pancreatitis (41.9%).

Elevated serum amylase levels can be observed with several medical and surgical problems in patients with

acute abdominal pain, but high values are usually associated with acute inflammatory pancreatic and gallbladder conditions, with very high levels in the former, making it one of the important diagnostic tools that can be used by health-care providers when evaluating patients suspected to have acute pancreatitis or acute calculous cholecystitis.

Keywords: Acute abdominal pain, Serum amylase, Diagnosis, Acute pancreatitis, Acute calculous cholecystitis, Sensitivity, Specificity.

1. INTRODUCTION

There is no standard global definition that can be used for all patients present with acute abdominal pain to the emergency department, but it can include any pain in the abdomen presenting acutely to health-care facilities (usually less than 5 days until presentation to consultation) requiring urgent management in the form of admission, giving parenteral fluid, analgesics prescription, ordering investigations and/or performing surgical interventions. In the United Kingdom (UK), it accounts nearly for 7-10% of all emergency department (ED) visits annually. Several abdominal and extra-abdominal conditions contribute to its pathophysiology. These conditions can be inflammatory, infective, obstructive, or ischemic in origin [1].

Diagnostic approach begins with thorough history taking and clinical examination that may give a clue of the provisional diagnosis in up to 50% of cases, adding laboratory investigations may raise the diagnostic yield, to reach 60% approximately. Several laboratory studies can be utilized for this purpose depending on the site, duration, and the pain character, and associated symptoms, taking into account patients past medical, surgical, social and gynecologic history. Routine testing, in spite of the cost-effectiveness issue, with Complete Blood Count (CBC) and urinalysis may direct the next orders by the physician in form of hematological, serological, biochemical, and often hormonal studies, mostly due to normal test results ordered at the first time. Addition of radiological tests (X-ray, ultrasound U/S, Computed Tomography CT, and/or Magnetic Resonance imaging MRI) may then follow. Yet, the diagnosis may not be clear in up to 30-40%, and 31% acute abdomen patients in the ED are considered to be non-specific abdominal pain, and it is more frequent in women. Non-specific abdominal pain is a diagnosis of exclusion and should be made only after thorough assessment by the surgeon on call in the ED in order not to miss any acute surgical or medical problems that can be source of threat to patient's life, either instantly or on the long term [1, 2].

Serum amylase is one of the biochemical investigations used most frequently by physicians when acute pancreatitis is suspected because of its availability, rapidity, and being inexpensive, although it may be elevated in several extra-pancreatic pathologies but at different magnitude.

Pancreatic digestive enzymes, especially amylase and lipase, are leaking into the circulation in small quantities under normal circumstances but in acute pancreatitis there will be major leakage and high serum amylase and lipase can be of diagnostic value [3].

Amylase or alpha-amylase, what is found in human body, is a calcium-dependent endoglycosidase that hydrolyses complex carbohydrates (amylose and amylopectin) into oligo disaccharides, and optimally functions at PH of 6.9-7 with a half-life of about ten to twelve hours. Liver is the main site of amylase removal, and only 3% of plasma amylase is filtered via kidneys, of which 25% is excreted, and majority reabsorbed in the proximal tubules. It has a molecular weight of 50K Daltons. Serum amylase exists in two isoenzyme sub-types:

1. Pancreatic amylase (P-amylase); synthesized by pancreatic acinar cells and secreted via pancreatic duct to the lumen of duodenum in its active form. Represents 35-50% of normal serum amylase.
2. Salivary amylase (S-amylase); produced by the salivary glands, which initiates its action in the oral cavity and terminates by acid in stomach, and found in smaller amounts in ovaries, fallopian tubes, lungs, and adipose tissue.

S-type amylase increases after birth to reach its adult value by two years of age, while P-amylase is not detected in most children before 6 months of age and starts to rise to reach adult values at 5 years of life, reflecting developing exocrine pancreas. Low values can be seen in pancreatic exocrine insufficiency as in chronic pancreatitis. When testing the serum sample for amylase, it can be stored at room temperature for up to 4 days with relatively stable amylase activity[4-6].

Urinary amylase level is also available in laboratory and can be used when the patient presents with acute abdominal pain but it has lower specificity, the only advantage was its availability at the bedside and being a rapid test to perform which also applies to serum amylase, subsequently its use was largely abandoned in practice [6].

There is variation in amylase level between different races, and age groups. Individuals of African and Asian descent have higher values due to unexplained increase in S-amylase. Serum amylase was noted to be greater in males and females over 60 years old that might be related to a decreased renal clearance in this age group [5].

Our study aims to evaluate the role of serum amylase measurement in adult patients presented with non-traumatic acute abdominal pain to the emergency department within the first twenty-four hour of consultation and admission, correlate our findings with time to consult, patients age and gender, try to look for those conditions cause high serum values more frequent than the others, and what makes a statistically significant rise of its level. High values may be found in the first 24 hour but this does not exclusively reflect pancreatic pathology, because other extra-pancreatic conditions also cause elevation in serum amylase but at lower amplitude compared to that of acute pancreatitis, as mentioned in literature.

2. METHODS

Our study conducted depending on data collected from patient's medical records in the emergency department of Shar teaching hospital including all adult patients, above sixteen years of age, admitted to surgical emergency department (ED) with complaint of non-traumatic abdominal pain, over a period of four months and twenty days, between 10th January 2019 and 20th May 2019, started within 24-hour of presentation to ED, only 68 patients were included whose diagnosis was clear on discharge from hospital, serum amylase level test was obtained within 1-2 hours of admission using ELISA technique at the laboratory division of ED and documented. Normal serum amylase level was set at 35-115IU/L. Patients included in this research were divided into 3 groups according to duration of symptoms before admission, as follows; first are those before 6 hours, second is between 6 to 12 hours, and the last are admitted after 12 hours but before 24 hours. Totally, eight diagnostic categories were identified in the patients (table2). For the purpose of being more accurate, the serum amylase level is further split to two groups, levels between 35-115 IU/L, the normal range and the second are those above 115IU/L. Additional tests were used to reach a definitive diagnosis including serum lipase level, radiologic studies like chest and abdominal X-ray, abdominal ultrasound (U/S) and CT of abdomen, and upper oesophago-gastro-duodenoscopy (OGD). Correlation between serum amylase levels, patient's time to presentation, age, gender, and definitive diagnosis was made. Study limitations include a small sample size because of short time period, inclusion of only those patients in whom a definite diagnosis was made, and lack of facility to measure P-amylase or S-amylase separately when required, so total serum amylase is used for all.

3. RESULTS

For the purpose of simplicity, our study results have been put into the following tables.
The patients were divided by the duration of their symptoms before admission into three groups as shown in (table 1). Patients presented after twenty-four hour were not included.

Table 1

Duration	Frequency	Percent
0-6 hours	27	39.7
6-12 Hours	35	51.5
12-24 Hours	6	8.8
Total	68	100.0

The frequency and percentage of patients ages are included in (table 2)

Table 2

Age groups	Frequency	Percent
Less than 60 years	55	80.9
More than 60 years	13	19.1
Total	68	100

These patients were diagnosed with various surgical diseases, eight diagnostic categories overall, at a different frequency, presented in (table 3)

Table 3

Diagnosis	Frequency	Percent
Acute pancreatitis	13	19.1
Acute calculous cholecystitis	14	20.6
Perforated peptic ulcer	3	4.4
Acute appendicitis	1	1.5
Intestinal obstruction	5	7.4
Symptomatic gallstone	14	20.6
Gastro-duodenitis	14	20.6
Peptic ulcer disease (PUD)	4	5.9
Total	68	100

Diagnosis of acute pancreatitis was made depending on the presence of two out of three of the following; patient symptoms and signs, including upper or diffuse abdominal pain that might

be radiating to the back, and be associated with vomiting, with other symptoms reported by the patient suggestive of acute pancreatitis, rise in serum amylase level three times the upper limit, supported by rise in serum lipase level, and radiologic features seen on ultrasound U/S of abdomen and contrast-enhanced CT abdomen, but not necessarily in all patients, performed in the following three to four days of admission, or when diagnosis was in doubt.

Acute calculous cholecystitis and symptomatic gallstone were diagnosed by clinical features and findings on abdominal U/S. Perforated peptic ulcer was diagnosis based on sudden acute abdominal pain, hemodynamic changes, rigid abdomen on palpation, air under the diaphragm on erect chest X-ray, and intra-operative finding of the perforation.

In cases of intestinal obstruction, patient's clinical findings and dilated loops of bowel on imaging guided the physician toward the pathology, and CT of abdomen and pelvis was utilized in some cases. While for the patient with suspected acute appendicitis the conclusion reached by interpreting modified Alvarado score together with gross intra-operative appearance of the appendix, confirmed by the histopathological report by the examining pathologist. OGD was used to prove PUD or gastro-duodenitis in clinically suspected cases.

The relation between patients gender and serum amylase level is demonstrated in (table 4)

Table 4

			Serum amyalse level		P value
			35 - 115	More than 115	
Gender	Male	Count	14	10	0.7
		Percent	37.8%	32.3%	
	Female	Count	23	21	
		Percent	62.2%	67.7%	
Total		Count	37	31	
		Percent	100.0%	100.0%	

Table 5 correlates the duration of acute abdominal pain with elevation in serum amylase level.

Table 5

			Serum amylase level		P value
			35 - 115	More than 115	
Duration	0-6 Hours	Count	10	17	0.03
			27.0%	54.8%	
	6-12 Hours	Count	22	13	
			59.5%	41.9%	
	12-24 Hours	Count	5	1	
			13.5%	3.2%	
Total		Count	37	31	
			100.0%	100.0%	

Table 6 reveals the relation between measured serum amylase and different age groups.

Table 6

			Serum amylase		P value
			35 - 115	More than 115	
Recode age	Less than 60 years	Count	30	25	0.9
		%	81%	80.6%	
	More than 60 years	Count	7	6	
		37	18.9 %	19.4%	
Total		Count	100. 0%	31	

The scope of serum amylase elevation is categorized into two groups, the first are those who were normal (35-115 IU/L), and the second whose serum amylase is above 115 IU/L. It is put into (table 7)

Table 7

Amyalse range		Frequency	Percent
	35 – 115 IU/L	37	54.4
	More than 115 IU/L	31	45.6
	Total	68	100.0

The next table (table 8) demonstrates how each relevant surgical diagnosis in this study affects the serum amylase level.

Table 8

			amyalse		P value
			35 - 115	More than 115	
Diagnosis	Acute pancreatitis	Count	0	13	<0.001
		%	0.0 %	41.9%	
	Acute calculous cholecystitis	Count	1	13	
		%	2.7 %	41.9%	
	Perforated Peptic ulcer	Count	1	2	
		%	2.7	6.5%	

			%		
	Acute appendicitis	Count	1	0	
		%	2.7 %	0.0%	
	Intestinal obstruction	Count	3	2	
		%	8.1 %	6.5%	
	Symptomatic gallstone	Count	14	0	
		%	37.8 %	0.0%	
	Gastro-duodenitis	Count	14	0	
		%	37.8 %	0.0%	
	PUD	Count	3	1	
		%	8.1 %	3.2%	
Total		Count	37	31	
		%	100.0%	100.0 %	

4. DISCUSSION

Overall, 68 patients included with mean (SD) age of 45.97±16.15 years, minimum and maximum ages were 20 and 86 respectively, Forty-four female (64.7%) and twenty-four male (35.3) patients. Fifty-five of them were under 60 years of age and the reminders thirteen were above that age. Normal serum amylase values was observed in thirty seven patients (14 males and 23 females), while ten men and twenty-one women had high amylase titers, totaling thirty one cases, and resultant p-value of 0.7 indicating that gender does not have an important impact when serum amylase test is undertaken.

Regarding patients age, twenty-five out of fifty-five patients had raised serum amylase were younger than 60 years, meanwhile those of 60 years or older were 13 cases with only 6 having elevated amylase, also pointing to that age of patients is insignificant (p-value 0.9).

An important influence on the frequency of amylase increment is time of presentation of the patients to hospital, as amylase rises quick, within (3-6 hours) of symptomatic commencement, and stays elevated for 3 to 7 days. In our study serum amylase level was high during the first six hours of symptoms in seventeen, in the next six hours in thirteen, and the following 12 hours in just a patient, which determines a great effect of time with elevation of serum amylase level (p-value 0.03), such finding is consistent with a study done by Basnayake et al., [7]which also supports a rapid increase within the first 3-6 hours of symptoms, but can return to normal after twenty-four hours due to the fact of a relative short half-life (10-12 hours). This finding is consistent with another study by Ghimire and colleagues [8] in Katmandu Medical College, in which highest values of serum amylase was noted in the first twenty-four hours.

Different diagnosis (table 7) contributed to increased serum amylase levels, thirty-one out of the sixty-eight patients in the study found to have hyperamylasemia, including all the thirteen acute pancreatitis cases, but except for acute pancreatitis no pathologic condition could raise it

more than three times its normal value, the amylase range for acute pancreatitis was 356-2627 IU/L.

At such threshold (three times the normal) the sensitivity and specificity of the test to diagnose acute pancreatitis is 75.2-100% and 93.5-100% respectively. Its positive predictive value and negative predictive value are both 100%, with diagnostic accuracy of 100%, closely similar to the results of a research by Ghimirie et al.,[8] sensitivity was 95.8% when amylase is more than 400 IU/L but drops to 85.2% when cut-off value is 1000 IU/L, but the specificity differs as it was 98.7% and 86.3% for the same amylase values, another difference was serum amylase values topped above 1000 IU/L in 1.1% of cases, that might be explained by a larger sample size compared to ours, 270 versus 68. Our findings are somewhat close to the results of Basnayake et al., with sensitivity 81-95%. [7, 8](Chamara Basnayake, Roshan Ghimirie)

A comparative study by Barbieri and colleagues between serum amylase and lipase for the diagnosis of acute pancreatitis showed superiority of lipase for the above mentioned purpose, since sensitivity of amylase was 78.7% and specificity to be 92.6% compared to lipase with sensitivity and specificity of 90.3% and 93%, respectively(5). Sutton et al. identified sensitivity (50%) and specificity (99%) for detecting acute pancreatitis at threshold of three times the normal range. [9]

Although serum amylase might result back normal in certain etiologies of pancreatitis like hypertriglyceridemia which interferes with laboratory testing itself and exocrine failure that can be seen in some patients with alcoholic pancreatitis or acute severe necrotizing pancreatitis. [10]

As recommended by The American College of Gastroenterology, presence of two out of the following three confirms diagnosis of acute pancreatitis; first is the acute abdominal pain consistent with the pain found in acute pancreatitis, elevation in serum amylase or lipase three times the upper limit, and characteristic radiologic findings on imaging (CT or MRI), contrast-enhanced CT is more favorable, but not performed for all patients, can be considered a significant tool when diagnosis is in doubt [4]

Probably the use of serum amylase in all of the sixty-eight patients with elevated values in 37 patients and three times rise in just 13 patients was to exclude acute pancreatitis and not to miss such grave diagnosis, that may result in considerable morbidity and mortality.

Fourteen patients suffering from acute calculous cholecystitis included in the study, thirteen of which found to have hyperamylasemia, equal in frequency to acute pancreatitis, mean value of 154 and the highest measure was 220 IU/L among them. Making its sensitivity to determine acute calculous cholecystitis 92.8% but with 66.67% specificity, the availability and sensitivity of abdominal U/S makes routine use of serum amylase in this group of patients unlikely of benefit, unless associated pancreatitis is suspected. Dynamic small intestinal

obstruction was the definitive diagnosis in 3 (8.1%), of which 2 had hyperamylasemia and perforated peptic ulcer diseases resulted in high amylase levels in 2 (13%) of patients, but the usual investigation in these patients are CT abdomen and serum lactate in the former group and an erect chest X-ray invaluable in the latter. Gastro-duodenitis was found in 14 cases (37.8%), for which OGD is the most useful investigation rather than serum amylase, based on the study results. Symptomatic gallstone was the diagnosis in fourteen patients, all had normal amylase level on testing. Only one patient admitted and diagnosed with acute appendicitis included in our study, whose amylase was within a normal range also, making the use of amylase clearly unreasonable. Three patients were diagnosed with PUD combining symptoms concordant with the disease process and use of OGD to confirm it later, one of them had elevated amylase value, so its use is of limited value.

A study conducted by Sutton et al. [11]was somewhat close to ours as it investigates the role of routine amylase and lipase measurement in acute abdominal pain including trauma patients, a total of 1520 patients were included with mean age of 49.6 years, 45.5% of which diagnosed with non-gastrointestinal diseases and considered inappropriate order of the tests, of the reminder 54.5% with gastrointestinal conditions, forty-four patients with acute pancreatitis were diagnosed and only 28 had high serum amylase and lipase, ultrasound and CT scan was

used to make a diagnosis of acute pancreatitis in the other 16 patients. Upper gastrointestinal diseases contributed to the forty-one false positive tests in the study, mostly caused by perforated peptic ulcer disease.

5. CONCLUSION

Acute abdominal pain is relatively a common presentation in the ED, apart from history and physical examination which both are crucial in diagnosis of any surgical or medical condition, other laboratory and radiological tests can be recruited to find the pathology. Serum amylase testing is frequently used, readily available, relatively cheap, and can be ordered if clinically justified, and it is widely acceptable if the patient presents within 5 days of symptoms. Although it lacks the specificity expected in order to differentiate intra-abdominal diseases but in comparison to other inflammatory markers such as CBC and C-reactive protein (CRP), amylase is a valuable tool when acute pancreatitis is suspected, once the level is three times the normal workup toward acute pancreatitis can be pursued.

Extra-pancreatic causes of acute abdominal pain may be implicated in raising serum amylase but the level would rarely be in the range of acute pancreatitis.

Finally we recommend reasonable use of serum amylase combined with the patient history and findings in physical examination, combined with other laboratory results, if the diagnosis is still unclear, additional radiological studies can be ordered if not already done by the surgical team.

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