



Acute pancreatitis – Is serum amylase still required?

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Acute pancreatitis – Is serum amylase still required?

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Running head: Lipase assay for pancreatitis

Key words: Pancreatitis, Pancreas, Lipase, Amylase

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Competing interests: None.

Contribution: Study design: Gomez, Brooks, Cameron; Data collection: Addison, De Rosa; Manuscript writing: Gomez, Addison, De Rosa, Brooks, Cameron

ABSTRACT

Objectives: To assess the role of serum amylase and lipase in the diagnosis of pancreatitis. Secondary aims were to perform a cost analysis of these enzyme assays in patients admitted to the surgical admissions unit.

Design: Cohort study, **Setting:** Secondary care

Participants: Patients admitted with pancreatitis to the acute surgical admissions unit from January – December 2010 were included in the study.

Methods: Data collated included demographics, laboratory results and aetiology. The cost of measuring a single enzyme assay was £0.69 and both assays were £0.99.

Results: Of the 151 patients included, 117 patients had acute pancreatitis with gallstones (n=51) as the most common cause. The majority of patients with acute pancreatitis had raised levels of both amylase and lipase. Raised lipase levels only were observed in additional 12% and 23% of patients with gallstone- and alcohol- induced pancreatitis, respectively. Overall, raised lipase levels were seen in between 95 – 100% of patients depending on aetiology. In patients with chronic pancreatitis (n=34), seven (22%) additional patients were diagnosed with alcohol-induced pancreatitis based on raised lipase levels. Sensitivity and specificity of lipase in the diagnosis of acute pancreatitis was 96.6% and 99.4%, respectively. In contrast, the sensitivity and specificity of amylase in diagnosing acute pancreatitis was 78.6% and 99.1%, respectively. Single lipase assay in all patients presenting with abdominal pain to the surgical admission unit would result in a potential saving of £893.70 per year.

Conclusion: Determining serum lipase level alone is sufficient to diagnose pancreatitis and substantial savings can be made if measured alone.

Article summary

Article Focus

1. Current guidelines suggest that lipase measurement is the most sensitive marker for diagnosing pancreatitis. Hence, do we still need to measure amylase levels?
2. Is this the case for both acute and chronic pancreatitis patients?
3. What is the effect on cost by measuring one enzyme level only?

Key Messages

1. Determining serum lipase level alone is sufficient to diagnose pancreatitis, especially in cases of acute pancreatitis.
2. Substantial savings can be made if lipase were measured alone.

Strengths

This manuscript focuses on a few important issues:

- a) Diagnosis: Lipase is more sensitive in diagnosing pancreatitis, irrespective of aetiology.
- b) Cost: There is no need to measure amylase, and all centres should measure lipase only.

Limitations

1. Single centre, retrospective study.

INTRODUCTION

The incidence of acute pancreatitis in the United Kingdom (UK) ranges from 150 to 420 cases per million population and is currently rising.^[1] In 80% of patients, acute pancreatitis is mild and resolves without serious morbidity, but in up to 20%, acute pancreatitis is complicated by substantial morbidity and mortality.^[2] Gallstone migration and alcohol abuse are the most common underlying aetiology, with gallstones being more frequently seen in women.^[3]

Traditionally, serum amylase was used to establish the diagnosis of pancreatitis, irrespective of aetiology. This test is particularly useful in patients presenting with acute abdominal pain to the Emergency Department or the acute surgical admissions unit to confirm the diagnosis of pancreatitis. Nevertheless, few studies have suggested that serum lipase is a more sensitive biomarker of acute pancreatitis compared to serum amylase.^[4, 5] The current British Society of Gastroenterology guidelines (2005) for the management of acute pancreatitis has also suggested a preference towards the measurement of lipase levels for the diagnosis of pancreatitis.^[6]

At present, due to the availability of both serum amylase and lipase, these tests are frequently requested concurrently in patients presenting with acute abdominal pain. The purpose of both these tests is to confirm the diagnosis of pancreatitis, irrespective of aetiology, although the levels of these enzymes have no correlation with the severity of the disease. The aim of the current study was to assess the clinical usefulness and diagnostic accuracy of serum amylase and lipase in the diagnosis of pancreatitis in the current patient population. Secondary aims were to perform a cost analysis of these enzyme levels of patients admitted with abdominal pain to the surgical admissions unit.

PATIENTS AND METHODS

Demographic data

Patients diagnosed with pancreatitis at the Queen’s Medical Centre Campus, Nottingham University Hospitals NHS Trust during the 1-year period, from January 2010 to December 2010, were identified using the hospital’s surgical emergency ward database. The medical data of these patients were prospectively reviewed through the hospital’s Nottingham Information System (NotIS). Data collected included demography, clinical presentation, laboratory studies, radiological investigations, underlying aetiology, timing of surgery and re-admission rates. Biochemical analyses recorded at presentation included serum amylase (reference range: 0 – 100 U/L) and lipase (reference range: 0 – 300 U/L), liver function tests [alanine aminotransferase (ALT, reference range: 0 – 45 U/L), alkaline phosphatase (ALP, reference range: 40 – 130 U/L) and total bilirubin (reference range: 0 – 21 µmol/L)], full blood count, urea and electrolytes, lactate dehydrogenase (LDH, reference range: 220 – 450 U/L) levels and calcium levels.

Diagnosis of Acute Pancreatitis

The diagnosis of pancreatitis was based on the following criteria: clinical features (abdominal pain and vomiting) together with the elevation of serum concentrations of pancreatic enzymes (amylase and / or lipase), a value three times greater than normal. At the time of this study, the practice in the Trust was to measure both serum amylase and lipase levels on admission in patients with acute abdominal pain.

All patients diagnosed with acute pancreatitis were then scored using the Glasgow Scoring System and had C-reactive protein (CRP) levels measured to predict the severity

of the attack.^[7, 8] Patients who had a Glasgow score of 3 or more or a CRP level >150 mg/l were predicted to have severe pancreatitis.

All patients underwent radiological imaging to identify gallstones. An abdominal ultrasound (USS) was usually the initial investigation. In cases where other acute abdominal pathology was suspected, an abdominal computer tomography (CT) scan was performed. Features to suggest an obstructed biliary system included the presence of dilated common bile duct on USS or CT. In cases with suspected common bile duct stones based on the presence of deranged liver function tests and / or dilated biliary tree on USS or CT, a magnetic resonance cholangio-pancreatography (MRCP) was performed. This unit's policy is to perform endoscopic retrograde cholangio-pancreatography (ERCP) only in cases with confirmed common bile duct stones on radiological imaging, or the presence of cholangitis in patients with acute pancreatitis.

Patients with a clinical history of high alcohol intake, with a negative USS result for gallstones were assumed to have alcohol-induced pancreatitis. The diagnostic criteria for chronic pancreatitis applied in this study were based on the Cambridge classification.^[9]

Cost analysis

The cost of a single pancreatic enzyme level (amylase or lipase) was £0.69 and the cost of both amylase and lipase levels when measured together were £0.99.

Statistical analysis

Non-parametric data is presented as median (range), and categorical data as both frequency and proportion (%). Sensitivity and specificity of serum amylase and lipase levels in diagnosing acute and chronic pancreatitis were calculated separately. Patients that did not have acute or chronic pancreatitis who had an elevation of three or more times the normal range of amylase or lipase were included in the specificity analysis. The cost of serum pancreatic enzymes measurement was determined in this patient cohort.

RESULTS

Demographic data

During the study period, 151 patients presented with pancreatitis to the surgical emergency unit, of which 117 (77.5%) patients were admitted with acute pancreatitis (Figure 1). There were 34 (22.5%) patients with a history of chronic pancreatitis. Ninety one (60%) patients were males, and the median age of presentation was 46 (17 – 90) years. There were 29 (19.2%) patients predicted to have severe pancreatitis based on the Glasgow Scoring System. The overall median length of hospital stay was 3 (2 – 90) days, with fourteen patients having intensive care and / or high dependency support during their admission. There were three in-patient deaths.

Aetiology

The underlying aetiology for patients with acute pancreatitis were gallstones (n = 51, 43.6%), alcohol (n = 22, 18.8%), idiopathic (n = 37, 31.6%), drug-induced (n = 4, 3.4%), pancreatic tumour (n = 2, 1.7%) and trauma (n = 1, 0.9%). With respect to chronic pancreatitis admission (n = 34), the majority of cases were associated with alcohol abuse (n=31, 91%).

Amylase and Lipase levels

The majority of patients with acute pancreatitis had raised levels of both amylase and lipase (n = 113, 97%). Raised lipase only was observed in additional 12% and 23% of patients with gallstone and alcohol related pancreatitis, respectively. Overall, raised lipase levels were seen between 95 – 100% of patients based on aetiology (Table 1).

There were no patients with pancreatitis in this cohort that had an elevated amylase level with a normal lipase level.

With respect to patients with alcohol-related chronic pancreatitis, seven (22%) additional patients were diagnosed based on raised lipase levels with concurrent normal amylase levels. However, the degree of enzyme elevation was less in chronic pancreatitis compared to acute pancreatitis.

A total of 2979 patients with acute abdominal pain were admitted to the surgical admission unit that had serum amylase and lipase measured. There were 18 patients that had an elevation of serum lipase more than three times the upper limit of normal that did not have pancreatitis. Twenty six patients that did not have pancreatitis had an elevation of serum amylase. All these patients had pancreatitis excluded by CT imaging that detected other pathology. With respect to patients admitted with acute pancreatitis, the overall sensitivity and specificity of serum lipase levels in diagnosing pancreatitis was 96.6% and 99.4%, respectively. In comparison to serum amylase levels, the overall sensitivity and specificity in diagnosing acute pancreatitis was 78.6% and 99.1%, respectively. In patients with chronic pancreatitis, the overall sensitivity and specificity of serum lipase levels was 64.7% and 99.4%, respectively. In contrast, the overall sensitivity and specificity of serum amylase levels in this patient group was 64.7% and 99.0%, respectively.

Cost analysis

The cost of measuring both enzyme levels in patients with pancreatitis was £149.49, compared to £104.19 if serum lipase was measured alone (saving £45.30 per

year). The total cost of measuring both pancreatic enzymes in all patients (n = 2979) admitted with acute abdominal pain through the surgical admissions unit was £2949.21. In contrast, the cost of measuring serum lipase only was £2055.51, a potential saving of £893.70.

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DISCUSSION

Accuracy of amylase and lipase levels

The current British Society of Gastroenterology guidelines for the management of acute pancreatitis suggest that clinical presentation with elevation of plasma concentration of pancreatic enzymes, preferably lipase levels, is the cornerstone of diagnosis.^[6] Various studies have demonstrated that serum lipase levels have better sensitivity and specificity compared to serum amylase levels in diagnosing pancreatitis.^[5, 10] Apple *et al.* observed that the sensitivity and specificity of serum lipase levels in the diagnosis of acute pancreatitis were 85% to 100% and 84.7% to 99.0%, respectively.^[4] Although Agrawal and co-workers observed a high sensitivity of serum amylase in the diagnosis of pancreatitis of 95 – 100%, the specificity (70%) was poor.^[5] The groups of Agrawal^[5] and Thomson^[10] reported a higher sensitivity and specificity in serum lipase levels for the diagnosis of acute pancreatitis when compared to serum amylase levels. Other authors have also observed similar results.^[11, 12] In the present study, the overall sensitivity and specificity of serum lipase and amylase levels in diagnosing acute pancreatitis was similar to previous published results. Although the majority of patients with acute pancreatitis had raised levels of both amylase and lipase, raised lipase levels with associated normal amylase concentrations was observed in an additional 12% and 23% of patients with gallstone and alcohol related pancreatitis, respectively. Hence, patients with pancreatitis would have potentially been missed if serum amylase alone was measured. A high specificity reported in this study may be due to the strict inclusion of only patients without pancreatitis that had an elevation of three times the upper limit of the normal range of pancreatic enzymes. Nevertheless, the above results suggest that

measurement of serum lipase levels forms an important part of the diagnostic work-up of patients suspected of having acute pancreatitis, especially in cases where the serum amylase concentrations are normal. However, in patients with chronic pancreatitis an elevation of the serum pancreatic enzyme levels are not always observed and clinical and radiological correlation are required in most cases to achieve a diagnosis.

Aetiology and pancreatic enzymes

Both amylase and lipase are released from acinar cells during acute pancreatitis, and their concentration in the serum is used to confirm diagnosis.^[13] However, the diagnosis of pancreatitis should not solely be based on the arbitrary value of three or four times greater than normal of pancreatic enzymes, but interpreted together with the clinical presentation.^[14] Amylase levels generally rise within a few hours after the onset of symptoms and return to normal values within 3 – 5 days, as it has a shorter half-life than lipase. However, amylase levels may remain within normal range in 19% of patients admitted with acute pancreatitis.^[15, 16] In addition, serum amylase levels may be elevated in the absence of acute pancreatitis in patients with decreased glomerular filtration, in diseases of the salivary glands, and in abdominal conditions associated with inflammation, including acute appendicitis, cholecystitis, intestinal obstruction or ischaemia, peptic ulcer disease and gynaecological pathology.^[17]

In contrast to serum amylase, serum lipase concentration is considered a more valuable diagnostic tool, because abnormally elevated values persist for a longer duration, which is an advantage in patients with a delayed presentation.^[18] In addition, serum lipase is more sensitive in terms of detecting the presence of acute alcohol-induced

pancreatitis.^[19] The present study demonstrated that raised lipase levels were seen in 95 – 100% of patients depending on aetiology. Seven (22%) additional patients were diagnosed with acute alcohol-induced pancreatitis based on raised lipase levels with an associated normal amylase level. Furthermore, the current UK^[6] and Japanese^[20] guidelines for the management of acute pancreatitis have emphasised the greater diagnostic accuracy of serum lipase compared to amylase. We would conclude that in agreement with other published studies,^[4, 21] that the combined use of serum amylase and lipase levels does not facilitate the accurate diagnosis of acute pancreatitis.

Cost

The measurement of serum amylase level is still more widely available compared to serum lipase level, and in hospitals where lipase assay is available, both pancreatic enzymes are measured.^[21] Clearly, the cost of two similar tests seems difficult to justify if they are essentially equivalent and lipase assay appear to be more accurate and clinically useful. In the present study, potentially £893.70 could have been saved over 1-year in patients admitted with acute abdominal pain to the surgical admissions unit. The potential savings observed in this study underestimates the true cost of both amylase and lipase assays as patients admitted in the Accident and Emergency department and Medical Admissions Unit were not included. At a national level, the potential savings would be a larger amount, with no loss of diagnostic accuracy. At present, it is estimated that acute pancreatitis is responsible for around 25,000 hospital admissions in England, and there is an increase in incidence annually. In just this group of patients, potentially £7500 could be saved annually.

Conclusion

In conclusion, measurement of serum lipase concentrations alone is sufficient to diagnose patients with pancreatitis and substantial savings can be made if measured alone.

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LEGENDS

Table 1: Levels of amylase and lipase with respect to underlying aetiology of acute and chronic pancreatitis.

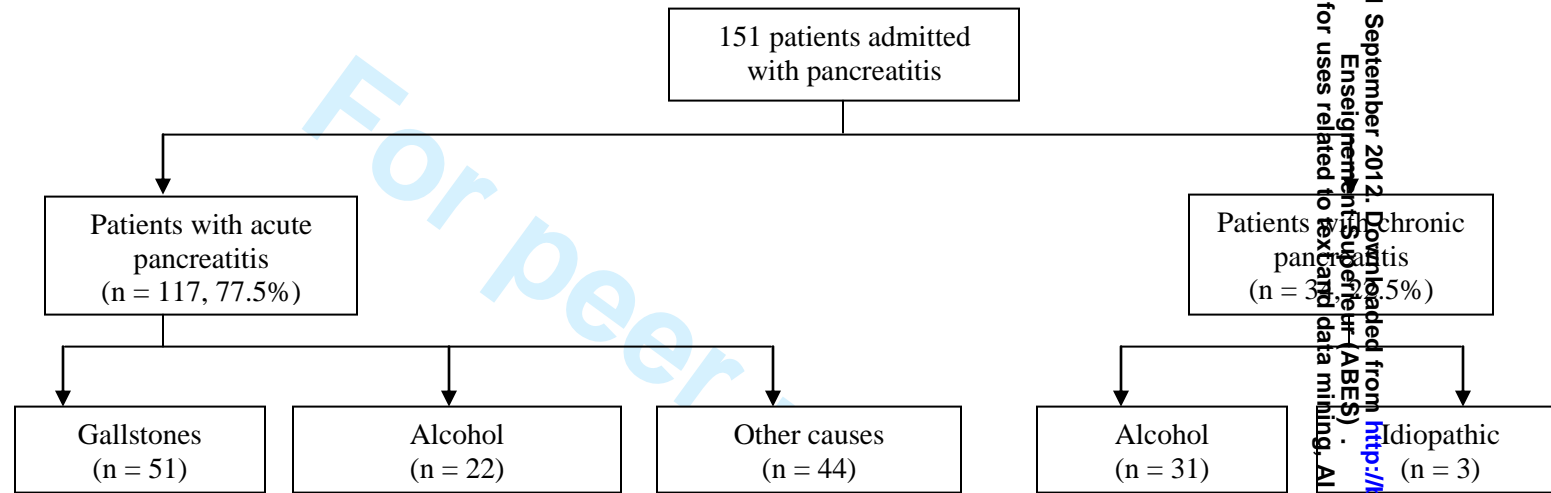
Figure 1: Aetiology of patients admitted with pancreatitis in this study.

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Table 1

Pancreatitis (n = 151)	Raised lipase and amylase levels	Raised lipase with normal amylase levels	Normal lipase and amylase levels	Overall raised lipase levels
Acute (n = 117)				
Gallstone (n = 51)	43 (84%)	6 (12%)	2 (4%)	49 (96%)
Alcohol (n = 22)	17 (77%)	5 (23%)	0 (0%)	22 (100%)
Other causes				
Idiopathic (n = 37)	28 (76%)	7 (19%)	2 (5%)	35 (95%)
Drug-induced (n = 4)	4 (100%)	0 (0%)	0 (0%)	4 (100%)
Tumour (n = 2)	0 (0%)	2 (100%)	0 (0%)	2 (100%)
Trauma (n = 1)	0 (0%)	1 (100%)	0 (0%)	1 (100%)
Chronic (n = 34)				
Alcohol (n = 31)	12 (39%)	7 (22%)	12 (39%)	19 (61%)
Idiopathic (n = 3)	2 (67%)	1 (33%)	0 (0%)	3 (100%)

Figure 1



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28 **Re: Acute pancreatitis – Is serum amylase still required?**
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33 journal.
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37 All the authors have approved the manuscript. There is no conflict of interest.
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41 If there is any further information you require, please contact us.
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44 Thank you for your cooperation.
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Reviewer: 1

1. This is a retrospective series questioning the need for the measurement of both serum lipase and amylase in diagnosing pancreatitis amongst patients presenting with abdominal pain. The authors correctly show that only 1 test is required and this is the normal practice in most UK institutions. The benefit of serum lipase over amylase appear marginal and in cases of diagnostic uncertainty the role of CT scanning provides additional information that is both diagnostic and predictive of subsequent outcome.

We agree with the above. However, most centres in the UK still use amylase only or both amylase and lipase measurements in patients with a differential diagnosis of pancreatitis. Hence, this manuscript aims to address this, emphasising that only one measurement (lipase only) is required, irrespective of the aetiology of pancreatitis.

Reviewer: 2

Comments to the Author

1. This study explores amylase and lipase measurement in pancreatitis and considers potential cost savings of a single test strategy (already used in many institutions). The authors base a diagnosis of acute pancreatitis on clinical features with an elevation of enzymes on test results recorded at admission. UK guidelines would suggest consideration should be given to interpreting the enzymes in the light of the time of onset of the pain. Despite this definition of acute pancreatitis four patients have normal lipase and amylase levels (Table 1). In these four patients, patients had normal levels of amylase and / or lipase levels, and the diagnosis of pancreatitis was achieved through radiological imaging.

2. I am unclear how sensitivities and specificities have been calculated.

Please refer to page 7, Statistical analysis section.

3. Neither the conclusion with respect to lipase nor the consideration of the cost implications is new hence a more extensive discussion of previous work in order to set this work in context might be advantageous.

This has been done, please see discussion section.



Retrospective study of patients with acute pancreatitis – Is serum amylase still required?

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Funding: This project received no specific grant from funding agency in the public, commercial or not-for-profit sectors.

Competing interests: None.

Contribution: Study design: Gomez, Brooks, Cameron; Data collection: Addison, De Rosa; Manuscript writing: Gomez, Addison, De Rosa, Brooks, Cameron

Data Sharing Statement

no additional data.

ABSTRACT

Objectives: To assess the role of serum amylase and lipase in the diagnosis of acute pancreatitis. Secondary aims were to perform a cost analysis of these enzyme assays in patients admitted to the surgical admissions unit.

Design: Cohort study, **Setting:** Secondary care

Participants: Patients admitted with pancreatitis to the acute surgical admissions unit from January – December 2010 were included in the study.

Methods: Data collated included demographics, laboratory results and aetiology. The cost of measuring a single enzyme assay was £0.69 and both assays were £0.99.

Results: Of the 151 patients included, 117 patients had acute pancreatitis with gallstones (n=51) as the most common cause. The majority of patients with acute pancreatitis had raised levels of both amylase and lipase. Raised lipase levels only were observed in additional 12% and 23% of patients with gallstone- and alcohol- induced pancreatitis, respectively. Overall, raised lipase levels were seen in between 95 – 100% of patients depending on aetiology. Sensitivity and specificity of lipase in the diagnosis of acute pancreatitis was 96.6% and 99.4%, respectively. In contrast, the sensitivity and specificity of amylase in diagnosing acute pancreatitis was 78.6% and 99.1%, respectively. Single lipase assay in all patients presenting with abdominal pain to the surgical admission unit would result in a potential saving of £893.70 per year.

Conclusion: Determining serum lipase level alone is sufficient to diagnose acute pancreatitis and substantial savings can be made if measured alone.

Article summary

Article Focus

1. Current guidelines suggest that lipase measurement is the most sensitive marker for diagnosing pancreatitis. Hence, do we still need to measure amylase levels?
3. What is the effect on cost by measuring one enzyme level only?

Key Messages

1. Determining serum lipase level alone is sufficient to diagnose acute pancreatitis.
2. Substantial savings can be made if lipase were measured alone.

Strengths

This manuscript focuses on a few important issues:

- a) Diagnosis: Lipase is more sensitive in diagnosing acute pancreatitis, irrespective of aetiology.
- b) Cost: There is no need to measure amylase, and all centres should measure lipase only.

Limitations

1. Single centre, retrospective study.

INTRODUCTION

The incidence of acute pancreatitis in the United Kingdom (UK) ranges from 150 to 420 cases per million population and is currently rising.^[1] In 80% of patients, acute pancreatitis is mild and resolves without serious morbidity, but in up to 20%, acute pancreatitis is complicated by substantial morbidity and mortality.^[2] Gallstone migration and alcohol abuse are the most common underlying aetiology, with gallstones being more frequently seen in women.^[3]

Traditionally, serum amylase was used to establish the diagnosis of pancreatitis, irrespective of aetiology. This test is particularly useful in patients presenting with acute abdominal pain to the Emergency Department or the acute surgical admissions unit to confirm the diagnosis of pancreatitis. Nevertheless, few studies have suggested that serum lipase is a more sensitive biomarker of acute pancreatitis compared to serum amylase.^[4, 5] The current British Society of Gastroenterology guidelines (2005) for the management of acute pancreatitis has also suggested a preference towards the measurement of lipase levels for the diagnosis of pancreatitis.^[6]

At present, due to the availability of both serum amylase and lipase, these tests are frequently requested concurrently in patients presenting with acute abdominal pain. The purpose of both these tests is to confirm the diagnosis of pancreatitis, irrespective of aetiology, although the levels of these enzymes have no correlation with the severity of the disease. The aim of the current study was to assess the clinical usefulness and diagnostic accuracy of serum amylase and lipase in the diagnosis of pancreatitis in the

current patient population. Secondary aims were to perform a cost analysis of these enzyme levels of patients admitted with abdominal pain to the surgical admissions unit.

PATIENTS AND METHODS

Demographic data

Patients diagnosed with acute pancreatitis at the Queen’s Medical Centre Campus, Nottingham University Hospitals NHS Trust during the 1-year period, from January 2010 to December 2010, were identified using the hospital’s surgical emergency ward database. The medical data of these patients were prospectively reviewed through the hospital’s Nottingham Information System (NotIS). Data collected included demography, clinical presentation, laboratory studies, radiological investigations, underlying aetiology, timing of surgery and re-admission rates. Biochemical analyses recorded at presentation included serum amylase (reference range: 0 – 100 U/L) and lipase (reference range: 0 – 300 U/L), liver function tests [alanine aminotransferase (ALT, reference range: 0 – 45 U/L), alkaline phosphatase (ALP, reference range: 40 – 130 U/L) and total bilirubin (reference range: 0 – 21 µmol/L)], full blood count, urea and electrolytes, lactate dehydrogenase (LDH, reference range: 220 – 450 U/L) levels and calcium levels.

Diagnosis of Acute Pancreatitis

The diagnosis of pancreatitis was based on the following criteria: clinical features (abdominal pain and vomiting) together with the elevation of serum concentrations of pancreatic enzymes (amylase and / or lipase), a value three times greater than normal. At

the time of this study, the practice in the Trust was to measure both serum amylase and lipase levels on admission in patients with acute abdominal pain.

All patients diagnosed with acute pancreatitis were then scored using the modified Glasgow Scoring System and had C-reactive protein (CRP) levels measured to predict the severity of the attack.^[7, 8] Patients who had a Glasgow score of 3 or more or a CRP level >150 mg/l were predicted to have severe pancreatitis.

All patients underwent radiological imaging to identify gallstones. An abdominal ultrasound (USS) was usually the initial investigation. In cases where other acute abdominal pathology was suspected, an abdominal computer tomography (CT) scan was performed. Features to suggest an obstructed biliary system included the presence of dilated common bile duct on USS or CT. In cases with suspected common bile duct stones based on the presence of deranged liver function tests and / or dilated biliary tree on USS or CT, a magnetic resonance cholangio-pancreatography (MRCP) was performed. This unit's policy is to perform endoscopic retrograde cholangio-pancreatography (ERCP) only in cases with confirmed common bile duct stones on radiological imaging, or the presence of cholangitis in patients with acute pancreatitis.

Patients with a clinical history of high alcohol intake, with a negative USS result for gallstones were assumed to have alcohol-induced pancreatitis.

Cost analysis

The cost of a single pancreatic enzyme level (amylase or lipase) was £0.69 and the cost of both amylase and lipase levels when measured together were £0.99.

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3 **Statistical analysis**
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6 Non-parametric data is presented as median (range), and categorical data as both
7 frequency and proportion (%). Sensitivity and specificity of serum amylase and lipase
8 levels in diagnosing acute and chronic pancreatitis were calculated separately. Patients
9 that did not have acute pancreatitis who had an elevation of three or more times the
10 normal range of amylase or lipase were included in the specificity analysis. The cost of
11 serum pancreatic enzymes measurement was determined in this patient cohort.
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RESULTS

Demographic data

During the study period, 151 patients presented with pancreatitis to the surgical emergency unit, of which 117 (77.5%) patients were admitted with acute pancreatitis (Figure 1). There were 34 (22.5%) patients with a history of chronic pancreatitis.

With respect to patients with acute pancreatitis, 68 (58%) patients were males, and the median age of presentation was 46 (17 – 90) years. There were 29 (19.2%) patients predicted to have severe pancreatitis based on the modified Glasgow Scoring System. The overall median length of hospital stay was 4 (2 – 90) days, with fourteen patients having intensive care and / or high dependency support during their admission. There were three in-patient deaths.

Aetiology

The underlying aetiology for patients with acute pancreatitis were gallstones (n = 51, 43.6%), alcohol (n = 22, 18.8%), idiopathic (n = 37, 31.6%), drug-induced (n = 4, 3.4%), pancreatic tumour (n = 2, 1.7%) and trauma (n = 1, 0.9%).

Amylase and Lipase levels

The majority of patients with acute pancreatitis had raised levels of both amylase and lipase (n = 113, 97%). Raised lipase only was observed in additional 12% and 23% of patients with gallstone and alcohol related pancreatitis, respectively. Overall, raised lipase levels were seen between 95 – 100% of patients based on aetiology (Table 1). There were no patients with pancreatitis in this cohort that had an elevated amylase level with a normal lipase level. Overall, there were four patients that had normal levels of both lipase and amylase, and these patients were diagnosed with acute pancreatitis following CT scan.

A total of 2979 patients with acute abdominal pain were admitted to the surgical admission unit that had serum amylase and lipase measured. There were 18 patients that had an elevation of serum lipase more than three times the upper limit of normal that did not have pancreatitis. Twenty six patients that did not have pancreatitis had an elevation of serum amylase. All these patients had pancreatitis excluded by CT imaging that detected other pathology (Table 2).

With respect to patients admitted with acute pancreatitis, the overall sensitivity and specificity of serum lipase levels in diagnosing pancreatitis was 96.6% and 99.4%, respectively. In comparison to serum amylase levels, the overall sensitivity and specificity in diagnosing acute pancreatitis was 78.6% and 99.1%, respectively.

Cost analysis

The cost of measuring both enzyme levels in patients with pancreatitis was £149.49, compared to £104.19 if serum lipase was measured alone (saving £45.30 per year). The total cost of measuring both pancreatic enzymes in all patients (n = 2979)

admitted with acute abdominal pain through the surgical admissions unit was £2949.21. In contrast, the cost of measuring serum lipase only was £2055.51, a potential saving of £893.70.

DISCUSSION

Accuracy of amylase and lipase levels

The current British Society of Gastroenterology guidelines for the management of acute pancreatitis suggest that clinical presentation with elevation of plasma concentration of pancreatic enzymes, preferably lipase levels, is the cornerstone of diagnosis.^[6] Various studies have demonstrated that serum lipase levels have better sensitivity and specificity compared to serum amylase levels in diagnosing pancreatitis.^[5, 9] Apple *et al.* observed that the sensitivity and specificity of serum lipase levels in the diagnosis of acute pancreatitis were 85% to 100% and 84.7% to 99.0%, respectively.^[4] Although Agrawal and co-workers observed a high sensitivity of serum amylase in the diagnosis of pancreatitis of 95 – 100%, the specificity (70%) was poor.^[5] The groups of Agrawal^[5] and Thomson^[9] reported a higher sensitivity and specificity in serum lipase levels for the diagnosis of acute pancreatitis when compared to serum amylase levels. Other authors have also observed similar results.^[10, 11] In the present study, the overall sensitivity and specificity of serum lipase and amylase levels in diagnosing acute pancreatitis was similar to previous published results. Although the majority of patients with acute pancreatitis had raised levels of both amylase and lipase, raised lipase levels with associated normal amylase concentrations was observed in an additional 12% and

23% of patients with gallstone and alcohol related pancreatitis, respectively. Hence, patients with pancreatitis would have potentially been missed if serum amylase alone was measured. A high specificity reported in this study may be due to the strict inclusion of only patients without pancreatitis that had an elevation of three times the upper limit of the normal range of pancreatic enzymes. Nevertheless, the above results suggest that measurement of serum lipase levels forms an important part of the diagnostic work-up of patients suspected of having acute pancreatitis, especially in cases where the serum amylase concentrations are normal.

Aetiology and pancreatic enzymes

Both amylase and lipase are released from acinar cells during acute pancreatitis, and their concentration in the serum is used to confirm diagnosis.^[12] However, the diagnosis of pancreatitis should not solely be based on the arbitrary value of three or four times greater than normal of pancreatic enzymes, but interpreted together with the clinical presentation.^[13] Amylase levels generally rise within a few hours after the onset of symptoms and return to normal values within 3 – 5 days, as it has a shorter half-life than lipase. However, amylase levels may remain within normal range in 19% of patients admitted with acute pancreatitis.^[14, 15] In addition, serum amylase levels may be elevated in the absence of acute pancreatitis in patients with decreased glomerular filtration, in diseases of the salivary glands, and in abdominal conditions associated with inflammation, including acute appendicitis, cholecystitis, intestinal obstruction or ischaemia, peptic ulcer disease and gynaecological pathology.^[16]

In contrast to serum amylase, serum lipase concentration is considered a more valuable diagnostic tool, because abnormally elevated values persist for a longer duration, which is an advantage in patients with a delayed presentation.^[17] In addition, serum lipase is more sensitive in terms of detecting the presence of acute alcohol-induced pancreatitis.^[18] The present study demonstrated that raised lipase levels were seen in 95 – 100% of patients depending on aetiology. Seven (22%) additional patients were diagnosed with acute alcohol-induced pancreatitis based on raised lipase levels with an associated normal amylase level. Furthermore, the current UK^[6] and Japanese^[19] guidelines for the management of acute pancreatitis have emphasised the greater diagnostic accuracy of serum lipase compared to amylase. Although there is good published literature with respect to measurement of lipase levels alone in diagnosing acute pancreatitis, this practice is still not observed in many UK centers. One possible explanation is the easy availability of assessment of amylase levels by local chemical pathology laboratories.²⁰ In addition, some authors have proposed that both tests are necessary to effectively diagnose pancreatitis,²¹ while other state that it is not necessary to perform both for diagnostic purposes.²² Although lipase levels are considered to be specific for acute pancreatitis, non-specific elevations of lipase have been reported in almost as many disorders as amylase, thus decreasing its specificity. We would conclude that in agreement with other published studies,^[4, 23] that the combined use of serum amylase and lipase levels does not facilitate the accurate diagnosis of acute pancreatitis.

Cost

The measurement of serum amylase level is still more widely available compared to serum lipase level, and in hospitals where lipase assay is available, both pancreatic

enzymes are measured.^[23] Clearly, the cost of two similar tests seems difficult to justify if they are essentially equivalent and lipase assay appear to be more accurate and clinically useful. In the present study, potentially £893.70 could have been saved over 1-year in patients admitted with acute abdominal pain to the surgical admissions unit. The potential savings observed in this study underestimates the true cost of both amylase and lipase assays as patients admitted in the Accident and Emergency department and Medical Admissions Unit were not included. At a national level, the potential savings would be a larger amount, with no loss of diagnostic accuracy. At present, it is estimated that acute pancreatitis is responsible for around 25,000 hospital admissions in England, and there is an increase in incidence annually. In just this group of patients, potentially £7500 could be saved annually.

Conclusion

In conclusion, measurement of serum lipase concentrations alone is sufficient to diagnose patients with pancreatitis and substantial savings can be made if measured alone.

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LEGENDS

Table 1: Levels of amylase and lipase with respect to underlying aetiology of acute pancreatitis.

Table 2: Conditions that caused raised levels of lipase and amylase.

Figure 1: Aetiology of patients admitted with pancreatitis in this study.

Table 1

Acute Pancreatitis (n = 117)	Raised lipase and amylase levels	Raised lipase with normal amylase levels	Normal lipase and amylase levels	Overall raised lipase levels
Gallstone (n = 51)	43 (84%)	6 (12%)	2 (4%)	49 (96%)
Alcohol (n = 22)	17 (77%)	5 (23%)	0 (0%)	22 (100%)
Other causes				
Idiopathic (n = 37)	28 (76%)	7 (19%)	2 (5%)	35 (95%)
Drug-induced (n = 4)	4 (100%)	0 (0%)	0 (0%)	4 (100%)
Tumour (n = 2)	0 (0%)	2 (100%)	0 (0%)	2 (100%)
Trauma (n = 1)	0 (0%)	1 (100%)	0 (0%)	1 (100%)

Table 2

Pathology	Raised lipase and amylase levels (n = 12)	Raised lipase with normal amylase levels (n = 6)	Raised amylase with normal lipase levels (n = 14)
Ruptured abdominal aortic aneurysm	7	3	5
Perforated duodenal ulcer	4	2	4
Cholecystitis	0	0	2
Intestinal obstruction	1	1	3

Retrospective study of patients with acute pancreatitis – Is serum amylase still required?

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Contribution: Study design: Gomez, Brooks, Cameron; Data collection: Addison, De Rosa; Manuscript writing: Gomez, Addison, De Rosa, Brooks, Cameron

ABSTRACT

Objectives: To assess the role of serum amylase and lipase in the diagnosis of [acute](#) pancreatitis. Secondary aims were to perform a cost analysis of these enzyme assays in patients admitted to the surgical admissions unit.

Design: Cohort study, **Setting:** Secondary care

Participants: Patients admitted with pancreatitis to the acute surgical admissions unit from January – December 2010 were included in the study.

Methods: Data collated included demographics, laboratory results and aetiology. The cost of measuring a single enzyme assay was £0.69 and both assays were £0.99.

Results: Of the 151 patients included, 117 patients had acute pancreatitis with gallstones (n=51) as the most common cause. The majority of patients with acute pancreatitis had raised levels of both amylase and lipase. Raised lipase levels only were observed in additional 12% and 23% of patients with gallstone- and alcohol- induced pancreatitis, respectively. Overall, raised lipase levels were seen in between 95 – 100% of patients depending on aetiology. ~~In patients with chronic pancreatitis (n=34), seven (22%) additional patients were diagnosed with alcohol-induced pancreatitis based on raised lipase levels.~~ Sensitivity and specificity of lipase in the diagnosis of acute pancreatitis was 96.6% and 99.4%, respectively. In contrast, the sensitivity and specificity of amylase in diagnosing acute pancreatitis was 78.6% and 99.1%, respectively. Single lipase assay in all patients presenting with abdominal pain to the surgical admission unit would result in a potential saving of £893.70 per year.

Conclusion: Determining serum lipase level alone is sufficient to diagnose [acute](#) pancreatitis and substantial savings can be made if measured alone.

Article summary

Article Focus

1. Current guidelines suggest that lipase measurement is the most sensitive marker for diagnosing pancreatitis. Hence, do we still need to measure amylase levels?

~~2. Is this the case for both acute and chronic pancreatitis patients?~~

3. What is the effect on cost by measuring one enzyme level only?

Key Messages

1. Determining serum lipase level alone is sufficient to diagnose [acute](#) pancreatitis; ~~especially in cases of acute pancreatitis.~~
2. Substantial savings can be made if lipase were measured alone.

Strengths

This manuscript focuses on a few important issues:

- a) Diagnosis: Lipase is more sensitive in diagnosing [acute](#) pancreatitis, irrespective of aetiology.
- b) Cost: There is no need to measure amylase, and all centres should measure lipase only.

Limitations

1. Single centre, retrospective study.

INTRODUCTION

The incidence of acute pancreatitis in the United Kingdom (UK) ranges from 150 to 420 cases per million population and is currently rising.^[1] In 80% of patients, acute pancreatitis is mild and resolves without serious morbidity, but in up to 20%, acute pancreatitis is complicated by substantial morbidity and mortality.^[2] Gallstone migration and alcohol abuse are the most common underlying aetiology, with gallstones being more frequently seen in women.^[3]

Traditionally, serum amylase was used to establish the diagnosis of pancreatitis, irrespective of aetiology. This test is particularly useful in patients presenting with acute abdominal pain to the Emergency Department or the acute surgical admissions unit to confirm the diagnosis of pancreatitis. Nevertheless, few studies have suggested that serum lipase is a more sensitive biomarker of acute pancreatitis compared to serum amylase.^[4, 5] The current British Society of Gastroenterology guidelines (2005) for the management of acute pancreatitis has also suggested a preference towards the measurement of lipase levels for the diagnosis of pancreatitis.^[6]

At present, due to the availability of both serum amylase and lipase, these tests are frequently requested concurrently in patients presenting with acute abdominal pain. The purpose of both these tests is to confirm the diagnosis of pancreatitis, irrespective of aetiology, although the levels of these enzymes have no correlation with the severity of

the disease. The aim of the current study was to assess the clinical usefulness and diagnostic accuracy of serum amylase and lipase in the diagnosis of pancreatitis in the current patient population. Secondary aims were to perform a cost analysis of these enzyme levels of patients admitted with abdominal pain to the surgical admissions unit.

PATIENTS AND METHODS

Demographic data

Patients diagnosed with [acute](#) pancreatitis at the Queen's Medical Centre Campus, Nottingham University Hospitals NHS Trust during the 1-year period, from January 2010 to December 2010, were identified using the hospital's surgical emergency ward database. The medical data of these patients were prospectively reviewed through the hospital's Nottingham Information System (NotIS). Data collected included demography, clinical presentation, laboratory studies, radiological investigations, underlying aetiology, timing of surgery and re-admission rates. Biochemical analyses recorded at presentation included serum amylase (reference range: 0 – 100 U/L) and lipase (reference range: 0 – 300 U/L), liver function tests [alanine aminotransferase (ALT, reference range: 0 – 45 U/L), alkaline phosphatase (ALP, reference range: 40 – 130 U/L) and total bilirubin (reference range: 0 – 21 μ mol/L)], full blood count, urea and electrolytes, lactate dehydrogenase (LDH, reference range: 220 – 450 U/L) levels and calcium levels.

Diagnosis of Acute Pancreatitis

The diagnosis of pancreatitis was based on the following criteria: clinical features (abdominal pain and vomiting) together with the elevation of serum concentrations of

pancreatic enzymes (amylase and / or lipase), a value three times greater than normal. At the time of this study, the practice in the Trust was to measure both serum amylase and lipase levels on admission in patients with acute abdominal pain.

All patients diagnosed with acute pancreatitis were then scored using the [modified](#) Glasgow Scoring System and had C-reactive protein (CRP) levels measured to predict the severity of the attack.^[7, 8] Patients who had a Glasgow score of 3 or more or a CRP level >150 mg/l were predicted to have severe pancreatitis.

All patients underwent radiological imaging to identify gallstones. An abdominal ultrasound (USS) was usually the initial investigation. In cases where other acute abdominal pathology was suspected, an abdominal computer tomography (CT) scan was performed. Features to suggest an obstructed biliary system included the presence of dilated common bile duct on USS or CT. In cases with suspected common bile duct stones based on the presence of deranged liver function tests and / or dilated biliary tree on USS or CT, a magnetic resonance cholangio-pancreatography (MRCP) was performed. This unit's policy is to perform endoscopic retrograde cholangio-pancreatography (ERCP) only in cases with confirmed common bile duct stones on radiological imaging, or the presence of cholangitis in patients with acute pancreatitis.

Patients with a clinical history of high alcohol intake, with a negative USS result for gallstones were assumed to have alcohol-induced pancreatitis. ~~The diagnostic criteria for chronic pancreatitis applied in this study were based on the Cambridge classification.~~^[9]

Cost analysis

The cost of a single pancreatic enzyme level (amylase or lipase) was £0.69 and the cost of both amylase and lipase levels when measured together were £0.99.

Statistical analysis

Non-parametric data is presented as median (range), and categorical data as both frequency and proportion (%). Sensitivity and specificity of serum amylase and lipase levels in diagnosing acute and chronic pancreatitis were calculated separately. Patients that did not have acute ~~or chronic~~ pancreatitis who had an elevation of three or more times the normal range of amylase or lipase were included in the specificity analysis. The cost of serum pancreatic enzymes measurement was determined in this patient cohort.

RESULTS

Demographic data

During the study period, 151 patients presented with pancreatitis to the surgical emergency unit, of which 117 (77.5%) patients were admitted with acute pancreatitis (Figure 1). There were 34 (22.5%) patients with a history of chronic pancreatitis.

With respect to patients with acute pancreatitis, 68~~Ninety-one~~ (58~~60~~%) patients were males, and the median age of presentation was 46 (17 – 90) years. There were 29 (19.2%) patients predicted to have severe pancreatitis based on the modified Glasgow Scoring System. The overall median length of hospital stay was 34 (2 – 90) days, with fourteen patients having intensive care and / or high dependency support during their admission. There were three in-patient deaths.

Aetiology

The underlying aetiology for patients with acute pancreatitis were gallstones (n = 51, 43.6%), alcohol (n = 22, 18.8%), idiopathic (n = 37, 31.6%), drug-induced (n = 4, 3.4%), pancreatic tumour (n = 2, 1.7%) and trauma (n = 1, 0.9%). ~~With respect to chronic~~

pancreatitis admission (n = 34), the majority of cases were associated with alcohol abuse (n=31, 91%).

Amylase and Lipase levels

The majority of patients with acute pancreatitis had raised levels of both amylase and lipase (n = 113, 97%). Raised lipase only was observed in additional 12% and 23% of patients with gallstone and alcohol related pancreatitis, respectively. Overall, raised lipase levels were seen between 95 – 100% of patients based on aetiology (Table 1). There were no patients with pancreatitis in this cohort that had an elevated amylase level with a normal lipase level. Overall, there were four patients that had normal levels of both lipase and amylase, and these patients were diagnosed with acute pancreatitis following CT scan.

~~With respect to patients with alcohol-related chronic pancreatitis, seven (22%) additional patients were diagnosed based on raised lipase levels with concurrent normal amylase levels. However, the degree of enzyme elevation was less in chronic pancreatitis compared to acute pancreatitis.~~

A total of 2979 patients with acute abdominal pain were admitted to the surgical admission unit that had serum amylase and lipase measured. There were 18 patients that had an elevation of serum lipase more than three times the upper limit of normal that did not have pancreatitis. Twenty six patients that did not have pancreatitis had an elevation of serum amylase. All these patients had pancreatitis excluded by CT imaging that detected other pathology (Table 2).

With respect to patients admitted with acute pancreatitis, the overall sensitivity and specificity of serum lipase levels in diagnosing pancreatitis was 96.6% and 99.4%, respectively. In comparison to serum amylase levels, the overall sensitivity and specificity in diagnosing acute pancreatitis was 78.6% and 99.1%, respectively. ~~In patients with chronic pancreatitis, the overall sensitivity and specificity of serum lipase levels was 64.7% and 99.4%, respectively. In contrast, the overall sensitivity and specificity of serum amylase levels in this patient group was 64.7% and 99.0%, respectively.~~

Cost analysis

The cost of measuring both enzyme levels in patients with pancreatitis was £149.49, compared to £104.19 if serum lipase was measured alone (saving £45.30 per year). The total cost of measuring both pancreatic enzymes in all patients (n = 2979) admitted with acute abdominal pain through the surgical admissions unit was £2949.21. In contrast, the cost of measuring serum lipase only was £2055.51, a potential saving of £893.70.

DISCUSSION

Accuracy of amylase and lipase levels

The current British Society of Gastroenterology guidelines for the management of acute pancreatitis suggest that clinical presentation with elevation of plasma concentration of pancreatic enzymes, preferably lipase levels, is the cornerstone of

diagnosis.^[6] Various studies have demonstrated that serum lipase levels have better sensitivity and specificity compared to serum amylase levels in diagnosing pancreatitis.^[5, 95, 10] Apple *et al.* observed that the sensitivity and specificity of serum lipase levels in the diagnosis of acute pancreatitis were 85% to 100% and 84.7% to 99.0%, respectively.^[4] Although Agrawal and co-workers observed a high sensitivity of serum amylase in the diagnosis of pancreatitis of 95 – 100%, the specificity (70%) was poor.^[5] The groups of Agrawal^[5] and Thomson^[94] reported a higher sensitivity and specificity in serum lipase levels for the diagnosis of acute pancreatitis when compared to serum amylase levels. Other authors have also observed similar results.^[10, 11, 12] In the present study, the overall sensitivity and specificity of serum lipase and amylase levels in diagnosing acute pancreatitis was similar to previous published results. Although the majority of patients with acute pancreatitis had raised levels of both amylase and lipase, raised lipase levels with associated normal amylase concentrations was observed in an additional 12% and 23% of patients with gallstone and alcohol related pancreatitis, respectively. Hence, patients with pancreatitis would have potentially been missed if serum amylase alone was measured. A high specificity reported in this study may be due to the strict inclusion of only patients without pancreatitis that had an elevation of three times the upper limit of the normal range of pancreatic enzymes. Nevertheless, the above results suggest that measurement of serum lipase levels forms an important part of the diagnostic work-up of patients suspected of having acute pancreatitis, especially in cases where the serum amylase concentrations are normal. ~~However, in patients with chronic pancreatitis an elevation of the serum pancreatic enzyme levels are not always observed and clinical and radiological correlation are required in most cases to achieve a diagnosis.~~

Aetiology and pancreatic enzymes

Both amylase and lipase are released from acinar cells during acute pancreatitis, and their concentration in the serum is used to confirm diagnosis.^[12+3] However, the diagnosis of pancreatitis should not solely be based on the arbitrary value of three or four times greater than normal of pancreatic enzymes, but interpreted together with the clinical presentation.^[13+4] Amylase levels generally rise within a few hours after the onset of symptoms and return to normal values within 3 – 5 days, as it has a shorter half-life than lipase. However, amylase levels may remain within normal range in 19% of patients admitted with acute pancreatitis.^[14, 15+5, +6] In addition, serum amylase levels may be elevated in the absence of acute pancreatitis in patients with decreased glomerular filtration, in diseases of the salivary glands, and in abdominal conditions associated with inflammation, including acute appendicitis, cholecystitis, intestinal obstruction or ischaemia, peptic ulcer disease and gynaecological pathology.^[16+7]

In contrast to serum amylase, serum lipase concentration is considered a more valuable diagnostic tool, because abnormally elevated values persist for a longer duration, which is an advantage in patients with a delayed presentation.^[17+8] In addition, serum lipase is more sensitive in terms of detecting the presence of acute alcohol-induced pancreatitis.^[18+9] The present study demonstrated that raised lipase levels were seen in 95 – 100% of patients depending on aetiology. Seven (22%) additional patients were diagnosed with acute alcohol-induced pancreatitis based on raised lipase levels with an associated normal amylase level. Furthermore, the current UK^[6] and Japanese^[19+9] guidelines for the management of acute pancreatitis have emphasised the greater

diagnostic accuracy of serum lipase compared to amylase. Although there is good published literature with respect to measurement of lipase levels alone in diagnosing acute pancreatitis, this practice is still not observed in many UK centers. One possible explanation is the easy availability of assessment of amylase levels by local chemical pathology laboratories.²⁰ In addition, some authors have proposed that both tests are necessary to effectively diagnose pancreatitis,²¹ while other state that it is not necessary to perform both for diagnostic purposes.²² Although lipase levels are considered to be specific for acute pancreatitis, non-specific elevations of lipase have been reported in almost as many disorders as amylase, thus decreasing its specificity. We would conclude that in agreement with other published studies,^[4, 234, 24] that the combined use of serum amylase and lipase levels does not facilitate the accurate diagnosis of acute pancreatitis.

Cost

The measurement of serum amylase level is still more widely available compared to serum lipase level, and in hospitals where lipase assay is available, both pancreatic enzymes are measured.^[2324] Clearly, the cost of two similar tests seems difficult to justify if they are essentially equivalent and lipase assay appear to be more accurate and clinically useful. In the present study, potentially £893.70 could have been saved over 1-year in patients admitted with acute abdominal pain to the surgical admissions unit. The potential savings observed in this study underestimates the true cost of both amylase and lipase assays as patients admitted in the Accident and Emergency department and Medical Admissions Unit were not included. At a national level, the potential savings would be a larger amount, with no loss of diagnostic accuracy. At present, it is estimated

that acute pancreatitis is responsible for around 25,000 hospital admissions in England, and there is an increase in incidence annually. In just this group of patients, potentially £7500 could be saved annually.

Conclusion

In conclusion, measurement of serum lipase concentrations alone is sufficient to diagnose patients with pancreatitis and substantial savings can be made if measured alone.

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For peer review only

LEGENDS

Table 1: Levels of amylase and lipase with respect to underlying aetiology of acute and chronic pancreatitis.

Table 2: Conditions that caused raised levels of lipase and amylase.

Figure 1: Aetiology of patients admitted with pancreatitis in this study.

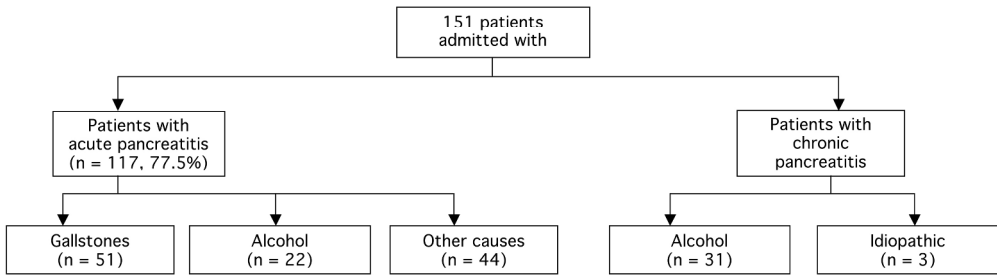
Table 1

<u>Acute</u> Pancreatitis (n = 11754)	Raised lipase and amylase levels	Raised lipase with normal amylase levels	Normal lipase and amylase levels	Overall raised lipase levels
Acute (n = 117)				
Gallstone (n = 51)	43 (84%)	6 (12%)	2 (4%)	49 (96%)
Alcohol (n = 22)	17 (77%)	5 (23%)	0 (0%)	22 (100%)
Other causes				
Idiopathic (n = 37)	28 (76%)	7 (19%)	2 (5%)	35 (95%)
Drug-induced (n = 4)	4 (100%)	0 (0%)	0 (0%)	4 (100%)
Tumour (n = 2)	0 (0%)	2 (100%)	0 (0%)	2 (100%)
Trauma (n = 1)	0 (0%)	1 (100%)	0 (0%)	1 (100%)
Chronic (n = 34)				
Alcohol (n = 31)	12 (39%)	7 (22%)	12 (39%)	19 (61%)
Idiopathic (n = 3)	2 (67%)	1 (33%)	0 (0%)	3 (100%)

Table 2

<u>Pathology</u>	<u>Raised lipase and amylase levels</u> (n = 12)	<u>Raised lipase with normal amylase levels</u> (n = 6)	<u>Raised amylase with normal lipase levels</u> (n = 14)
<u>Ruptured abdominal aortic aneurysm</u>	<u>7</u>	<u>3</u>	<u>5</u>
<u>Perforated duodenal ulcer</u>	<u>4</u>	<u>2</u>	<u>4</u>
<u>Cholecystitis</u>	<u>0</u>	<u>0</u>	<u>2</u>
<u>Intestinal obstruction</u>	<u>1</u>	<u>1</u>	<u>3</u>

Figure 1



240x80mm (300 x 300 DPI)

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Editor

BMJ Open Journal

9 August, 2012

Re: Retrospective study of patients with acute pancreatitis – Is serum amylase still required?

We would like to re-submit this manuscript titled above for publication in your journal.

All the authors have approved the manuscript.

If there is any further information you require, please contact us.

We would be grateful if the journal could consider a waiver for publication cost as we did not receive any funding for this project.

Thank you for your cooperation.

Yours sincerely,

Mr. Cameron

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From the managing editor

Please include the study design type in the title. At present, the title could be for a review or comment article.

We have done this – the title is now:

Retrospective study of patients with acute pancreatitis – Is serum amylase still required?

Reviewer 1:

There are a couple of minor points:

1. The authors should indicate what they used as a gold standard for diagnosis of AP against which the sensitivity and specificity of lipase and amylase were calculated.

The diagnosis of acute pancreatitis was based on clinical findings and biochemical tests, as per BSG guidelines. The value of three times greater than normal of lipase or amylase was considered diagnostic of pancreatitis following correlation with clinical findings.

Please see page 5, last para:

The diagnosis of pancreatitis was based on the following criteria: clinical features (abdominal pain and vomiting) together with the elevation of serum concentrations of pancreatic enzymes (amylase and / or lipase), a value three times greater than normal.

2. I suggest omitting the data on chronic pancreatitis from this paper as lipase and amylase are not routinely used for this purpose. I think that the authors should develop a larger series of patients with CP in which amylase and lipase have been measured to determine if, either alone or in combination, they can aid in the diagnosis of this condition.

We have omitted the data with respect to chronic pancreatitis (please see manuscript).

Reviewer 2:

This is a retrospective observational study describing the superiority of serum lipase over serum amylase in the diagnosis of acute pancreatitis. However, the authors have included both acute and chronic pancreatitis patients in the study cohort and this detracts from the conclusions of the study. Separation of the acute and chronic pancreatitis patients (or removal of the chronic pancreatitis patients), along with some minor restructuring of the manuscript would enhance the authors' message. Further, as the authors point out, the superiority of serum lipase over serum amylase in the diagnosis of acute pancreatitis is already well-described and recommended by various medical bodies; and this study supports that literature.

1. The diagnosis of chronic pancreatitis is not based on elevated serum amylase or lipase levels alone but also relies on symptoms and radiological imaging. Are the authors including acute on chronic pancreatitis patients as these patients probably represent a different spectrum/cohort of patients; and would be corroborated by the fact that the authors describe a reduced degree of enzyme elevation in chronic pancreatitis, as compared to acute pancreatitis? Separation

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of acute and chronic pancreatitis would be helpful in further delineating which patients should undergo measurement of serum lipase levels.

As suggested by Reviewer 1, we have removed the cohort of chronic pancreatitis patients (please see manuscript), and only included results from patients admitted with acute pancreatitis.

2. Do the authors have available data concerning time from symptom onset to presentation or assessment of serum amylase/lipase levels? A delay in presentation is likely to be an underlying factor behind the lack of elevated serum amylase levels in certain patients, given the quick peak and decrease in amylase levels in response to pancreatic injury.

We do not have data on symptom onset to presentation with respect to assessment of serum amylase/lipase levels. The aim of this study was to assess the diagnostic accuracy of serum amylase and lipase in the diagnosis of pancreatitis in patients at presentation, irrespective of onset of symptoms.

3. Was the Glasgow score used as described in the manuscript or was it the more commonly utilised Modified Glasgow scoring system? And what was the breakdown of the scores?

We did use the modified Glasgow scoring system (please see text, correction has been done). There were 29 patients who scored more than 3 *i.e.* predicted severe pancreatitis.

Please see page 6, line 4:

All patients diagnosed with acute pancreatitis were then scored using the modified Glasgow Scoring System and had C-reactive....

Please see page 8, para 2:

With respect to patients with acute pancreatitis, 68 (58%) patients were males, and the median age of presentation was 46 (17 – 90) years. There were 29 (19.2%) patients predicted to have severe pancreatitis based on the modified Glasgow Scoring System.....

4. Table 2 describes that there were two acute pancreatitis patients and one chronic pancreatitis patients with normal lipase and amylase levels - how were these patients diagnosed with pancreatitis?

We have removed patients with chronic pancreatitis from this study. With regards to four patients with normal amylase and lipase levels, they were diagnosed with radiological imaging (computer tomography).

Please see page 9, para 1:

..... Overall, there were four patients that had normal levels of both lipase and amylase, and these patients were diagnosed with acute pancreatitis following CT scan.

5. Further discussion of, or a basic table describing, the non-pancreatitis aetiologies that led to elevated serum amylase/lipase levels would be helpful to aid the reader in understanding the important differential diagnoses when using these serum assays.

A table has been done, please refer to Table 2.

Pathology	Raised lipase and amylase levels (n = 12)	Raised lipase with normal amylase levels (n = 6)	Raised amylase with normal lipase levels (n = 14)
Ruptured abdominal aortic aneurysm	7	3	5
Perforated duodenal ulcer	4	2	4
Cholecystitis	0	0	2
Intestinal obstruction	1	1	3

6. Given that a plethora of information already suggests that serum lipase levels are superior to serum amylase levels for the diagnosis of acute pancreatitis, and the assays are of similar cost, why are they not utilized in more UK centres? A discussion of the potential limitations of serum lipase assays and the underlying reasons for its lack of utilization would be useful.

This has been included in the discussion section.

Please see page 13, line 1:

..... Although there is good published literature with respect to measurement of lipase levels alone in diagnosing acute pancreatitis, this practice is still not observed in many UK centers. One possible explanation is the easy availability of assessment of amylase levels by local chemical pathology laboratories.²⁰ In addition, some authors have proposed that both tests are necessary to effectively diagnose pancreatitis,²¹ while other state that it is not necessary to perform both for diagnostic purposes.²² Although lipase levels are considered to be specific for acute pancreatitis, non-specific elevations of lipase have been reported in almost as many disorders as amylase, thus decreasing its specificity.