

The use of serum Amylase as a predictive factor for mortality in Perforated Duodenal Ulcer

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Abstract:

Background: High serum amylase is frequently found in perforated duodenal ulcer (PDU), the rise in serum amylase occurs in cases of perforated peptic ulcer partly as a result of increase leakage of pancreatic enzymes rich fluid from the perforation site with subsequent absorption by peritoneal lymphatics & partly due to damage of pancreases by digestive enzymes that spilled through the perforation.

Objectives: To determine the significance of abnormally high level of serum amylase in patients undergone operation for PDU, to study the factors that tend to bring about elevated serum amylase level in these patients.

Patients and Methods: A prospective study of 250 patients with perforated duodenal ulcer (PDU) at al kindy teaching hospital, Baghdad, Iraq from June 2008- august 2010. patients were examined clinically and investigated by blood test, chest x- ray, plain X- ray of the abdomen. & ultrasonography (U/S). Resuscitation by intravenous fluid, antibiotic were done. Explorative laparotomy performed for all patients, repair of perforation done by simple omental patch. Data regarding site, size of perforation, amount of spilled fluid and operative finding were recorded.

Results: Two hundred fifty patients included in this study with proven PDU, 222 (88.8 %) were male and 28 (11.2 %) were female, male to female ratio is 8 :1. The mean age was 38 years, ranging from 22-70 years. The over all mortality was 14.4%. In 210 patients(84%), the serum amylase was within normal range, the mortality in this group was 10 %. The other 21 patients (16%) had level of 200 or above, the mortality in this group was 37.5 %. Mortality was 5 % in cases with mild intra peritoneal fluid spillage, 9% in moderate, 25% in large amount & 39 in massive intra peritoneal spillage. The size of perforation has prognostic significance, for the larger the perforation, the higher the mortality.

Conclusions: Limiting surgical delay in patients with PDU seems to be of paramount importance in reducing the mortality in these patients. In patients with PDU, the high serum amylase the high mortality rate.

Keywords: PDU, serum amylase, mortality rate, time delay.

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Introduction:

Peptic ulcer disease (PUD) represents a worldwide health problem because of its high morbidity, mortality and economic loss². Globally, the incidence of peptic ulcer disease has fallen in recent years^{3,4}. Despite this and recent advances in both diagnosis and management of peptic ulcer disease, namely the improvement in endoscopic facilities, eradication of *H. pylori* and the introduction of the proton pump inhibitors, complications such as peptic ulcer perforation remain a substantial healthcare problem. This may be due to an increase in the risk factors for peptic ulcer complications^{1,4}. Peptic ulcer disease and its complications remains a frequent clinical problem in our environment predominantly affecting young males not known to suffer from PUD. Simple closure with omental patch followed by *Helicobacter pylori* eradication was effective with excellent results in majority of pts despite

patients' late presentation in our country. Peptic ulcer perforation is a serious complication which affects almost 2-10% of peptic ulcer patients on the average^{5,6}. Peptic ulcer perforation presents with an overall mortality of 10%⁹ although some authors report ranges between 1.3% and 20%^{8,9}. The most important factor in preventing the post operative morbidity and mortality in patients with PDU is the time factor, so that the shorter the interval between diagnosis and initiation of surgical treatment the less complication rate. A successful outcome could be obtained by prompt recognition of the diagnosis, aggressive resuscitation and early institution of surgical management. The pattern of perforated PUD has been reported to vary from one geographical area to another depending on the prevailing socio-demographic and environmental factors¹⁰. In the developing world, the patient population is young with male predominance, patients present late, and there is a strong association with smoking^{11,12}. The diagnosis of perforated DU poses a diagnostic challenge in most of cases. The spillage of duodenal or gastric contents into peritoneal cavity causing

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abdominal pain, shock, peritonitis, marked tenderness and decreased liver dullness offers little difficulty in diagnosis of perforations ¹³ Since the first description of surgery for acute perforated peptic ulcer disease, many techniques have been recommended. The recent advances in antiulcer therapy have shown that simple closure of perforation with omental patch followed by eradication of H. Pylori is a simple and safe option in many centers and have changed the old trend of truncal vagotomy and drainage procedures ¹⁵. Although surgery is normally the correct treatment for perforated duodenal ulcer, the whole patient and the comorbidity need to be taken into account. Perforations may seal themselves by adherence to liver, gallbladder, or omentum.

Patients and Methods:

This is a prospective study of 250 patients with PDU who attend to the emergency department and treated surgically with explorative laparotomy at Al-Kindy Teaching Hospital, Baghdad from period June 2008-August 2010. The diagnosis of PDU in all patients was based on the presence of history of acute epigastric pain with generalized tenderness and rebound tenderness with board like rigidity. The diagnosis supported by history of chronic dyspeptic symptoms, previous endoscopic finding of DU, with history of long-term ingestion of steroid or NSAID. Blood samples were aspirated from all patients to assess the level of serum amylase in addition to hemoglobin level, blood urea, serum sugar and serum electrolyte (Na⁺, K⁺) and serum Ca²⁺. The normal range of serum amylase in the peripheral circulation is considered to be 80-150 units (somogi) Most of references regard a release of 150, 160, 180 up to 200 somogi unit as upper limit of normal concentration of amylase in serum, in this study, in order to avoid inclusion of technical error, the range of normal was considered to extend to 200 unit

All patients were underwent U/S exam to demonstrate free intraperitoneal fluid. CXR in erect position were done for all patients to detect free gas under diaphragm, All patients underwent an exploratory laparotomy by midline incision under general anesthesia Data were collected by regarding the demographic information, the radiological, ultrasonography and operative finding, site of perforation, amount of spilled fluid, level of serum amylase by special performa. After preliminary resuscitation with IV fluid in form of crystalloid solution from 0.5 to 2 liters according to the general conditions of the patients and hydration state. Correction of electrolyte disturbance if present. Nasogastric tube inserted to all patients preoperatively. Foleys catheter inserted when indicated. Preoperative antimicrobial therapy given in form of third generation cephalosporin in the form of cefotaxime and metronidazole was used in all cases. Written consents were taken from all patients. All patients underwent explorative laparotomy by midline incision and some of patients (20 patients, 8%) by right paramedian incision. Identification of the site size and nature of the perforation done, closure of the perforation was done with omental patch (grahams

omentopexy) using 2/0 absorbable suture. Peritoneal lavage done by using 1-3 liters of warmed saline. 2 tube drain were inserted, 1st near the site of repair and second in the pelvis. The Wound was closed in layers. Patients were followed up during hospitalization and one month after discharging home and complications were recorded. The data were analyzed by computer using Minitab statistical software version 14, for analysis. P value of < 0.05 was considered statistically significant.

Results:

Two hundred fifty patients included in this study with proven PDU, 222 (88.8 %) male and 28 (11.2 %) female, male to female ratio is 8 : 1. The mean age was 38 years, ranging from 22-70 years.

PDU was noted to occur most commonly at the age group of 30-40 years and less frequently at other age group, as shown in table 1.

Table 1: Distribution of patients with PDU according to the different age groups

Age group	No. of pts	% of pts	M/F ratio (%)
20-29 yrs	44	17.6	40/4
30-39yrs	98	39.2	98/8
40-49yrs	53	21.2	53/5
50-59yrs	33	13.2	33/6
60 & above	22	8.8	22/5
total	250	100%	222/28

In 84 % (210 patients) of cases of PPU, the serum amylase was within normal range. The other 16% patients had level of 200 or above, these findings are summarized in table 2. The mortality for those patients who had essentially normal serum amylase was 10 %, while those with high serum amylase was ranging from 27.77 % - 80% .

Table 2: Serum amylase value in 250 cases of PDU Elevated serum amylase and abdominal fluid spill

Serum amylase Range (somogi)	No. of cases	% of cases	No. of death	Mortality rate
Up to 200	210	84 %	21	10 %
200-300	18	7.2 %	5	27.77 %
300-400	12	4.8 %	4	33.3 %
400-600	5	2 %	2	40 %
Over 600	5	2 %	4	80 %

For purpose of analysis, the cases in which the amount of fluid spill had been estimated roughly by the surgeon were grouped in categories (>250, 250-500, 500-1000, and >1000) ml. In general the greater the fluid spill, the higher the mortality rate.

In group with massive spill, the mortality was 55%. Higher serum amylase with large and massive amounts of abdominal

fluid were statistically companionate as shown in table 3. The mortality in group with large spill was double that in patients with small or moderate spill.

Table3: Amylase value in relation to amount of fluid spill in PDU Relation of duration of perforation to the serum amylase

Amount of spilled fluid	Total cases	Amylase level		No. of death (% of total)
		Normal	Elevated	
Small (less than 250 ml)	89	81	8	9.5 %
Moderate (250-500ml)	82	72	10	11 %
Large (500-1000ml)	56	45	11	19 %
Massive (more than 1000ml)	23	12	11	50 %

Eighty seven patients had a duration of perforation less than 8 hrs, in whom only 14% had high amylase, while 13 pts had duration of more than 48 hrs in whom 23% had high serum amylase as shown in table 4.

Table 4 : Duration & serum amylase level .Size of perforation

Duration (hrs)	Total cases	Normal amylase	Elevated amylase	%of elevation
0 – 8	87	75	12	13.8 %
8 - 16	108	93	15	13.8 %
16 - 24	26	19	7	26.9%
24 - 48	16	12	4	25 %
Over 48	13	10	3	23%

A strong correlation of the size of ulcer with amount of amylase was noted ($r=0.68$). The correlation was not constant, however in 4 cases in which perforations were 1.5-2 cm in diameter, the serum amylase level were within normal limits.

Discussion :

While peptic ulcer disease has decreased in incidence over the past decades, the epidemiological pattern of the complications, including hemorrhage and perforation, have changed little¹⁵. Although outcomes from bleeding ulcers have improved with modern endoscopic and interventional radiological Strategies¹⁶, the outcomes of perforations have remained fairly unchanged¹⁷. A number of scoring systems for outcome prediction have been reported, yet none appear to be superior and most are investigated in isolation. The Boey score was the first score directly aimed at mortality prediction for perforated peptic ulcer¹⁸. The original work by Boey et al stated that delay of surgery after onset of symptoms for more than 48 hours, shock upon admission and a high degree of co-

morbidity, were associated with a 100% mortality when all factors were present¹⁸. In many series, the mortality rates vary from 6.5% to as high as 20%^{19,20}. Mortality rates as high as 25–30 per cent also have been reported. The present study showed a mortality rate of 36[13.3%] out of 250 cases. Few attempts have been made to study the direct effect of serum amylase on the mortality but a lot of study analyze the factors that may tends to increase the level of serum amylase such as the size of perforation, time delay before surgery and amount of fluid spilled in the peritoneal cavity. The results revealed a strong correlation between the factors and serum amylase level so that the rise in serum amylase level is directly proportional the size of perforation, time interval before surgery and amount of peritoneal contamination and there is an agreement with other study done by Buck, et al.,²¹ in the present study, we found that these factors are interrelated and act as a precursors for high serum amylase, we study these factors separately. It is also known that the size of perforation is more likely associated with higher mortality and morbidity due to increased peritoneal contamination²². The present study showed the strong correlation between the amount of peritoneal contamination with high serum amylase level and thereby with high mortality (table 3), so that more than 50% of those with more than 1000 ml of spilled fluid into peritoneal cavity have raised serum amylase and mortality was 39 %, these findings was in agreement with other findings by other authors²³. In the current study, a strong correlation of the size of ulcer with amount of amylase was noted so that the larger size the perforation the higher amylase level and hence the higher mortality, between the correlation, however in many cases in which perforation size were 1.5-2 cm in diameter, the serum amylase level were within normal limits, furthermore, there is no clear cut definition for size of ulcer perforation even though the size less than 2.5cm carries good prognosis by simple closure with omental patch²⁴. These findings were in accordance with studies done in Italy and India by Syanes & Gupta et al.,^{24,25} Treatment delay in PPU is a well established negative prognostic factor²⁵. However, the evidence derives from studies with a high risk of bias²⁶, and no study has assessed the association between hourly surgical delay and adverse outcome²⁵. In our current work we found a dramatic rise in the mortality (26%) in those patients whom undergone surgery after more than 24 hrs of perforation, these results were identical to results obtained by other work²⁶.

Conclusions:

Serum amylase is not a specific enzyme in PDU, it may increase in many surgical diseases like pancreatitis, cholecystitis, in addition to PDU, but it may be considered a predictive factor for mortality. In this study we concluded that serum amylase is an essential factor that affect the outcome after surgery for PDU, all the factors which favors the production of increased serum amylase; the size of the perforation, the amount of fluid accumulation in the abdominal cavity and the duration of perforation those are also factors in increasing the

mortality from perforated ulcer. A successful outcome could be obtained by prompt recognition of the diagnosis, aggressive resuscitation and early institution of surgical management.

Authors Contribution:

Tawfiq J.M. Al-Marzooq & Dr.Ali Kareem Al-Majidi : Surgery , sample collection and writing.

Ragad E. Naji : Biochemical investigation, statistical analysis and writing.

.Yaser Abbas : Reference collection and writing.

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