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Ideal Predictors for the Severity of Acute Pancreatitis: A single center Egyptian study

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Abstract

Background & Aims: The ideal predictor of acute pancreatitis should be inexpensive, readily available in most emergency departments, easily applicable, consistent, non-invasive and has the statistical power. Although such predictor has not been detected, the research continues to pursue such one.

This survey was created to research and evaluate different simple laboratory tests as possible predictors of severe acute pancreatitis.

Materials and Methods: The study population consists of 40 patients admitted to the gastroenterology and Hepatology unit, Tanta University emergency hospital after being diagnosed to have acute pancreatitis. The following data were collected from all patients within 24 hours of admission: Age, sex, complete blood count, body mass index, blood glucose level, serum creatinine, blood urea nitrogen, total bilirubin, aspartate aminotransferase, C-reactive protein, total serum calcium, serum lipase and amylase, arterial blood gases, abdominal ultrasonography and chest X-ray.

Results: The study population consisted of 17 males and 23 females. The patients were being divided into two groups: group 1 that included 28 patients diagnosed as mild acute pancreatitis and group 2 that included 12 patients diagnosed as moderate to severe acute pancreatitis.

Blood glucose, BUN, AST, CRP, serum lipase, BMI, hematocrit value, leukocytes and platelets count showed significant P value on comparing the two groups. Area under the curve (AUC) had been calculated for the above mentioned possible predictors and it represents the overall accuracy of all points. Blood glucose, AST and platelets count showed the highest AUC, sensitivity, specificity, PPV, NPV and accuracy among other proposed predictors, However, other proposed predictors showed high NPV.

Conclusion: Blood glucose level, AST and platelets count showed the highest AUC, sensitivity, specificity, PPV, NPV and accuracy among other proposed predictors. Although other proposed predictors showed lower results than the above mentioned predictors, they still have a very significant NPV and can be used to rule out severe acute pancreatitis.

Introduction

Acute pancreatitis (AP) is best defined physiologically as an acute inflammatory process of the pancreas with variable involvement of other regional tissues or remote organ system, AP is a complex process in which pancreatic enzyme activation causes local pancreatic damage, resulting in an acute inflammatory response. AP is a common disorder that leads to large number of admissions in Egypt and elsewhere in the world (1,2).

Although the clinical course of AP is usually mild and resolves without sequelae, 20% of patients will experience a severe attack of AP resulting in a variety of systemic and local complications with significant increase in morbidity and mortality (3, 4).

The prediction of severity of AP is not only important for predicting the clinical course of the disease but also important for early admission of the patients to intensive care unit and identifying those at great risk of morbidity and

mortality for further management, more informed clinical decision making and even intervention to relieve the cause or treating the complications due to the disease process.

The severity of AP can be predicted using clinical, laboratory and radiologic risk factors, various grading systems and serum markers. No perfect system exists for predicting which patients will develop severe AP. The problem with all predictive models and systems is that they have low specificity when combined with the low prevalence of severe AP result in modest positive predictive values (5).

The ideal predictor should be fast, inexpensive, minimally invasive and can detect patients at low risk of complications (6). Although, no predictor has been proven to be the ideal one (5), some of these predictors show to be promising and of great value in predicting severe AP.

Many predictors have been studied before with varying results. Body mass Index (BMI), hematocrit value, blood glucose level and pleural effusion detected by plain chest radiograph are simple tests and promising predictors to the severity of AP and provide significant data for clinical decision making and proper management(7). However, some other predictors like total serum calcium level showed mixed results (7, 8).

In this study, we try to determine the most simple (easily applicable), accurate, inexpensive and rapid tests which can be used as predictors of severity of acute pancreatitis.

Patients and Methods:

This study included 40 patients admitted to the gastroenterology and the Hepatology unit during the period from January 2014 to December 2014, at Tanta University emergency hospital after being diagnosed to have acute pancreatitis.

AP was diagnosed clinically by a patient presenting with 2 of the following 3 criteria: (1) symptoms consistent with pancreatitis (e.g. epigastric pain), (2) a serum amylase or lipase level greater than 3 times the laboratory's upper limit of normal range, and (3) radiology imaging consistent with pancreatitis, usually using CT or MRI

All patients were being divided into 2 groups based on 2012 Atlanta Classification Revision of Acute Pancreatitis (9): Group 1, that were diagnosed as mild acute pancreatitis (no organ failure and no local or systemic complications), it included 28 patients, and group 2, that were diagnosed as moderate to severe acute pancreatitis (with single or multiple organ failure and/or local or systemic complications), it included 12 patients.

Organ failure was defined as having a score of 2 or more based on Modified Marshall scoring system for organ failure which was calculated on admission and at 48 hours after admission (10).

Patients have been excluded from the study in the following conditions: history of diabetes mellitus, admission after 24 hours from the start of the disease, history of pancreatic carcinoma or chronic pancreatitis, pregnancy, history of severe debilitating disease and history of illness that could compromise the interpretation of the investigations such as known anemia or pleural effusion prior to development of acute pancreatitis.

The ethics research committee, Faculty of Medicine, Tanta University has approved conduction of this study.

All patients were subject to the following that were performed at the time of admission within the initial 24 hours from the start of the disease: Complete history taking, complete clinical examination with recording of vital signs, calculation of body mass index, CBC, blood glucose level, serum creatinine, blood urea nitrogen (BUN), liver functions, C-reactive protein (CRP), total serum calcium, serum lipase and amylase, arterial blood gases, abdominal ultrasonography and plain chest radiography.

Statistical Analysis

Data were tabulated, coded then analysed using the computer program SPSS (Statistical package for social science) version 17.0. Data was presented as mean ± standard deviation for parametric data; median, minimum and maximum for non-parametric data and frequency for qualitative data.

Student's *t*-test was used to compare between mean of two groups of numerical (parametric) data. For continuous non-parametric data, Mann-Whitney *U*- test was used for inter-group analysis. Inter-group comparison of categorical data was performed by using chi square test (X^2-value)

The sensitivity and specificity of some parameters were examined at different cutoff points using receiver operating characteristic (ROC) curve analysis to determine the best cutoff point as well as the diagnostic power of each test. A *P* value <0.05 was considered statistically significant. And a *P* value <0.0001 was considered highly significant in all analyses.

Results

Table 1 shows age and gender of all studied patients in addition to the laboratory data that were done within initial 24 hours from the start of the disease.

Our results shows that no significant difference regarding ***age*** and sex among the two studied groups. Regarding body mass index (***BMI***), table 1 shows that group 2 with moderate

to severe AP had BMI significantly higher than that in group 1 with mild AP (p value = 0.005).

As regards the ***vital data analysis*** of the two groups, the mean±SD of body temperature in group 1 and group 2 was 37.92±2.91 and 39.03±0.35 respectively with a P value of 0.37 which shows no statistical significance. So, body temperature can't be used as reliable predictor of AP severity. On the other hand, there were a significant statistical difference between patients of group 1 and group 2 as regards heart rate, systolic and diastolic blood pressures (P value <0.001).

Blood glucose showed mean±SD of 125±25 mg/dL in the group 1 while it was 188±35 mg/dL in the group 2 with a P value of <0.001 which has high statistical significance. ***CRP*** showed mean±SD of 60±37 mg/L in the group 1 and 121±36 mg/L in the group 2 with a P value of 0.003 which is highly significant. ***Hematocrit value*** mean±SD was 37.2±4.1% in the group 1, while it was 45.3±7.3% in the group 2 with a P value of 0.005 which is highly significant. As regard ***total leucocytic count*** *and* ***platelets count***, the mean±SD of the group 1 was 10.6±2.3 K/mm^3 and 255±37 K/mm^3 respectively while in group 2 it was 15.6±5 K/mm^3 and 178±43 k/mm^3 respectively. The P value for leucocytic count was 0.006 while for the platelets count was 0.001 and both are considered highly significant.

Total serum calcium mean±SD of the group 1 was 2.07±0.32 mmol/L and for the group 2 was 2.38±1.04 mmol/L with a P value of 0.3 which is considered statistically insignificant. At the same time, ***Serum amylase*** mean±SD of the group 1 was 653.1±368.9 U/L and for the group 2 was 1054.2±714.9 U/L with a P value of 0.11 which is considered statistically insignificant. Both total serum calcium and serum amylase were ruled out as possible predictors of severity due to their insignificant P value.

BUN showed median of 31 mg/dL in the group 1 and 78.5 mg/dL for group 2 with a P value of 0.003 which is considered highly significant. Similarly, ***AST*** median in the group 1 was 60 U/L and in group 2, it was 153 with a P value of 0.001 which is highly significant. As for the ***serum lipase*** the median in the group 1 was 451.5 U/L and in group 2, it was 966.5 with a P value of 0.02 with is considered statistically significant. On the other hand, ***total bilirubin***, the median of group 1 was 1.74 mg/dL and 4.8 mg/dL in group 2 with a P value of 0.3 which is insignificant and thereby ruled out as a possible predictor of severity.

As regards local complications, all patients of group 2 showed peripancreatic fluid collection with no evidence of acute necrotic collection. As for systemic complications, all patients of group 2 had renal failure but only 8 patients of group 2 have pleural effusion and only 2 patients in group 2 had respiratory failure. (table2)

Ultrasonography was used to detect gall bladder stones and biliary mud as a possible cause for acute pancreatitis. Gall bladder stones and/or biliary mud had been confirmed to be present by ultrasonography in 14 patients in group 1 and 6 patients in group 2. Post ERCP acute pancreatitis had been found in one patient in group 2. The causing agent had not been identified in 14 patients in the first group and 5 patients in the second one. (table2)

Blood glucose, BUN, AST, CRP, serum lipase, BMI, hematocrit value, leucocytic and platelets counts were chosen for further statistical analysis as possible predictors of severity due to their significant P value. Area under the curve (AUC) had been calculated for the above mentioned possible predictors and it represents the overall accuracy of all points. With the area under the curve has been calculated, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and accuracy have been calculated with proposed cutoff values. From table 3, ***blood glucose***, ***AST*** and ***platelets count*** showed the highest AUC, sensitivity, specificity, PPV, NPV and accuracy among other proposed predictors and can be used as predictors of severe acute pancreatitis. However, other proposed predictors showed high NPV and can be used to rule out severe acute pancreatitis rather than confirming it.

Table 1: Patients Age, Gender and laboratory data.

Parameter	Group 1 (n=28)	Group 2 (n=12)	*P value*
Age (Years): Mean±SD	44± 16	48± 15	***0.6 (ns)***
Gender Male	12 (42.9%)	5 (41.7%)	***0.9 (ns)***
Female	16 (57.1%)	7 (58.3%)	
BMI: Median(range)	24.6 (24.1 - 26.8)	26.8 (24.6 - 27.8)	***0.005***
The vital data for all patients: Mean±SD			
• **Temperature (°C)**	37.92± 2.91	39.03± 0.35	***0.37(ns)***
• **Heart rate**	75.93± 7.14	99.00± 6.81	***<0.001***
• **SystolicBP (mm Hg)**	102.50 ±8.49	85.83± 5.85	***<0.001***

• DiastolicBP (mm Hg)	62.86± 5.08	49.17± 8.61	*<0.001*
Laboratory data for all patients			
• Blood Glucose(mg/dL) : Mean±SD	124±25	188±35	*<0.001*
• CRP(mg/L) : Mean±SD	60±37	121±36	*0.003*
• Hematocrit Value (%): Mean±SD	37.2±4.1	45.3±7.3	*0.005*
• Leucocytic Count(K/mm3) : Mean±SD	10.6±2.3	15.6±5	*0.006*
• Platelets count(K/mm3) : Mean±SD	255±37	178±43	*0.001*
• BUN(mg/dL) : Median(range)	31.0 (18.0 - 89.0)	78.5 (59.0 - 178.0)	*0.003*
• AST(U/L) : Median(range)	60 (20- 276)	153 (112- 276)	*0.001*
• Serum Lipase(U/L) : Median(range)	451.5 (90.1 - 1189)	966.5 (175.0 - 1593.0)	*0.02*
• Serum Amylase(U/L) : Mean±SD	653.1±368.9	1054.2±714.9	*0.11(ns)*
• Total Serum Calcium(mmol/L) : Mean±SD	2.07±0.32	2.38±1.04	*0.3 (ns)*
• Total Bilirubin(mg/dL) : Median(range)	1.74 (0.70 - 7.80)	4.80 (0.80 - 9.20)	*0.3 (ns)*

Table 2: Causes and complications of AP in all studied patients.

Parameter	Group 1 (n=28)	Group 2 (n=12)	*P value*
Causes of AP			
• Gall bladder stones and/or biliary mud	14	6	
• Post ERCP	0	1	
• Others	14	5	
Complications of AP			
• Peripancreatic fluid collection	0	12	
• Acute necrotic collection	0	0	
• Renal failure	0	12	
• Respiratory failure	0	2	
• Cardiovascular failure	0	0	
• Pleural effusion	0	8	

Table 3: AUC sensitivity, specificity, PPV, NPV and accuracy for proposed cutoff points.

	AUC	Cutoff value	Sensitivity	Specificity	PPV	NPV	Accuracy
Blood Glucose(mg/dL)	94.0%	154.0	83.3	85.7	71.4	92.3	85.00
BUN(mg/dL)	90.5%	59.5	83.3	78.6	62.5	91.7	80.00
AST(U/L)	93.5%	128	83.3	92.9	83.3	92.9	90.00
CRP(mg/L)	88.1%	88.5	83.3	78.6	62.5	91.7	80.00
Serum lipase(U/L)	83.3%	565	83.3	71.4	55.6	90.9	75.00
BMI	88.7%	25.05	83.3	71.4	55.6	90.9	75.00
Hematocrit value(%)	85.1%	40.5	83.3	78.6	62.5	91.7	80.00

Leucocytic count(K/mm^3)	82.7%	12.5	83.3	78.6	62.5	91.7	80.00
Platelets count (K/mm^3)	94.00%	195.5	83.3	92.9	83.3	92.9	90.00

Discussion

Accurate assessment of the incidence and mortality of acute pancreatitis is difficult as mild pancreatitis may be subclinical and deaths may occur before the diagnosis is made in severe and fulminant attacks. (12)

Predicting severity of pancreatitis early in the course of disease is critical to maximize therapy and to prevent and minimize organ dysfunction and complications. At the same time, it can help identify patients at increased risk for morbidity and mortality, thereby assisting in appropriate early admission to intensive care units and selection of patients for specific interventions. As severe acute pancreatitis may progress very rapid and is normally associated with a complicated clinical course and higher mortality, it is vital to identify these patients as early as possible to initiate appropriate supportive management, especially within the first 24 hours after symptoms begin (14).

The search for a tool that can improve on the clinical assessment and predicting the severity of acute pancreatitis has been ongoing for decades. A number of predictive models have been developed to predict the severity of acute pancreatitis based upon clinical, laboratory, and radiologic risk factors, various severity grading systems, and serum markers(6). However, these predictive models have low specificity which when coupled with the low prevalence of severe acute pancreatitis results in low positive predictive values (5).

The ideal tool should be simple, rapid inexpensive, noninvasive and easily applicable, can be performed as early as possible and have the statistical power to arrive to a valid conclusion accurately(15).

In this study, Gallstone-induced pancreatitis was identified in 20 patients, 14 in the first group and 6 in the second group. Post ERCP induced pancreatitis was identified in one patient in the second group while idiopathic pancreatitis was identified in 19 patients, 14 in the first group and 5 in the second group. The high number of idiopathic pancreatitis cases was due to absence of alcoholic pancreatitis as a main cause due to prohibition of alcohol intake by local regulations and difficult access to alcoholic beverages.

In the current study, blood glucose level showed a high statistical power with P value less than 0.001 with AUC of 94%. At a cutoff value 154 mg/dL sensitivity was 83.3%, specificity 85.7%, PPV 71.4%, NPV 92.3% and accuracy 85%. An elevated glucose level is associated with organ failure and severe acute pancreatitis and this is why the elevated glucose levels are higher in the severe group.

These results are supported by the studies performed by Zhang XY et al. and Zuo, Y.Y. et al. Zhang XY et al. concluded that elevated glucose is an indicator of organ failure and poor prognosis of severe acute pancreatitis (16). Zuo, Y.Y. et al. found a positive association of mean glucose level and glycemic liability index (as a measure of glucose variability) and mortality rate in severe acute pancreatitis patients (17).

In this study, Platelets count showed high statistical significance more than leucocytic count with P value 0.001 and 0.006 respectively. For **platelets count**, AUC was 94% at a cutoff value of 195.5 K/mm^3 with sensitivity 83.3%, specificity 92.2%, PPV 83.3%, NPV 92.9% and accuracy 90%. Platelets count was lower in the severe group due to their consumption in the systemic inflammatory process which is inversely proportionate to the extent of the inflammatory response to acute pancreatitis. For **leucocytic count**, AUC was 82.7% at a cutoff value of 12.5 K/mm^3 with sensitivity 83.3%, specificity 78.6%, PPV 62.5%, NPV 91.7% and accuracy 80%.Leucocytic count is directly proportionate to the extent of immune response and severity of the disease.

These results are backed up by the studies of Yoshinori Fujimura et al. and Mimidis K. et al. Yoshinori Fujimura et al. suggested that platelet count at admission and its change over the course of hospitalization can be useful measures for predicting prognosis in patients with acute pancreatitis. In addition, close attention must be paid to changes in the condition of any patient presented on admission with thrombocytopenia. They found platelets count less than 100 K/mm^{3}is associated with increased mortality at day 1 and day 5 (18). Mimidis K. et al. found that platelets count, function and indexes were altered by the severity of the disease and the decrease of platelets were associated with a severe course of the disease (19).

Regarding **AST** results, it showed a high statistical power with a P value of 0.001 with AUC 93.5%. At a cutoff value of 128 U/L sensitivity was 83.3%, specificity 92.9%, PPV 83.3%, NPV 92.9% and accuracy 90%.AST is an enzyme found primarily in the liver and heart, but it is also found in many other tissues including the muscle, red blood cells, pancreas, kidney, and brain. Damage to these organs or hemolysis releases the enzyme, resulting in elevated AST levels in the serum. Serum levels generally parallel to the extent of damage(20).

These results are consistent with that performed by Lin et al. and Liang, J. et al. Lin et al. identified initial common bile duct size and AST level as significant predictors of choledocholithiasis in biliary pancreatitis (21). Liang J. et al.

found that the increased levels of inflammatory mediators was correlated with liver damage in severe acute pancreatitis than the mild AP which explains the increased level of liver enzymes in the severe group more than the mild one (22).

In the current study, **BUN** level at admission showed P value of 0.003 with AUC 90.5%.at a cutoff value of 59.5mg/dL sensitivity was 83.3%, specificity 78.6%, PPV 62.5%, NPV 91.7% and accuracy 80%. The elevated BUN is correlated to the amount of third space fluid loss and decreased renal perfusion and/or function in relation to the severity of the disease. Hence, the more severe the attack of pancreatitis, the more the level of BUN is rising.

These study results are supported by two studies performed by Yang C.J. et al. and Wu B.U. et al. Yang C.J. et al. in a systematic review of literature in 3 databases of prospective studies, found that it is justifiable to use blood urea nitrogen for prediction of persistent organ failure after 48h of admission(23). In a large hospital-based cohort, Wu B.U.et al. found that serial BUN measurements were the most reliable routine laboratory test to predict the mortality in acute pancreatitis (24).

In the present study, **body mass index** (BMI) was used to evaluate obesity in the study patients. BMI showed considerable statistical significance (P value is 0.005) with AUC of 88.7%.At cutoff value of 25.05, sensitivity was 83.3%, specificity 71.4%, PPV 55.6%, NPV 90.9% and accuracy 75%. According to modern conceptions, obese people are in a state of chronic inflammation. Studies have shown that excess adipose tissue generates more leptin and resistin, and less adiponectin. This, in turn, leads to the prevalence of pro-inflammatory over anti-inflammatory cytokines, resulting in a state of constant inflammation of the adipose tissue (25). This explains why obesity has a negative impact on the course of acute pancreatitis and may lead to an attack of severe acute pancreatitis.

These results are supported by the study of Bonfrate L et al. who found that obesity is associated with increased incidence of gall stones and its complications including acute pancreatitis (26). A meta-analysis done by Shin K.Y. et al that included 739 patients showed that obesity is associated with more severe course of the disease, systemic complications, local complications and higher mortality rate than other groups (27).

Regarding C-reactive protein, it showed P value of 0.003 and AUC 88.1%. At a cutoff value of 88.5 mg/L sensitivity was 83.3%, specificity 78.6%, PPV 62.5%, NPV 91.7% and accuracy 80%.C-reactive protein (CRP) is one of the acute phase reactants made by the liver in response to interleukin-1 and interleukin-6. The CRP level is directly proportionate to the severity of the inflammatory process and this explains why CRP level is higher in the severe group than the mild group.

In agree with these results two studies performed by Wilson C et al. (28) and Ke, L. et al (29). Wilson C et al. showed that levels of CRP above 150mg/L at 48 hours discriminate severe from mild disease. At 48 hours, CRP above 150 mg/L has a sensitivity, specificity, positive predictive value, and negative predictive value of 80, 76, 67, and 86%, respectively, for severe acute pancreatitis. Ke L. et al. found that CRP when combined with measurement of intraabdominal hypertension was a good predictor of severity early after hospital admission.

In the current study, **hematocrit value** showed considerable statistical power (P value 0.006) with AUC 85.1%.At a cutoff value of 40.5% sensitivity was 83.3%, specificity 78.6%, PPV 62.5%, NPV 91.7% and accuracy 80%. Acute pancreatitis results in significant third space losses, resulting in hemoconcentration and a high hematocrit value. This shows that a high hematocrit value at admission is associated with high third space loss of fluids and a more severe course of acute pancreatitis.

These results showed similarity to the studies performed by Lankisch P.G. et al. (30) and Remes-Troche J.M. et al. (16) to evaluate the hematocrit as a predictor of the severity of AP have produced variable results. The discrepancies may be due to differences in values chosen as a cutoff and the time that they were obtained. Despite these differences, it appears that a normal or low hematocrit at admission and during the first 24 hours is generally associated with a milder clinical course.

Moreover, **Serum lipase** level in this study showed P value of 0.02 with AUC of 83.3%. At a cutoff value of 565 U/L sensitivity was 83.3%, specificity 71.4%, PPV 55.6%, NPV 90.9% and accuracy 75%. Serum lipase levels represent the extent of the inflammatory process in the pancreas and the severity of the disease.

These results are supported by the studies of Yadav D. et al. (31) and Coffey M.J. et al. (32). Yadav D. et al. found that serum lipase had sensitivity and specificity for diagnosis of acute pancreatitis ranging from 82 to 100%. Serum lipase rises within four to eight hours of the onset of symptoms, peaks at 24 hours, and returns to normal within 8 to 14 days. Lipase elevations occur earlier and last longer as compared with elevations in amylase and are therefore especially useful in patients who present >24 hours after the onset of pain(33). Coffey M.J. et al. found that rise of lipase level more than 7 folds than normal level was associated with severe course of the disease in children. However, this study results are contradicted by the study of Manes, G. et al. who found that serum lipase and amylase levels were not useful

in detecting the etiology or predicting the severity of acute pancreatitis (34).

In the current study, chest roentgenograms showing pleural effusion had a P value of 0.05 which is statistically insignificant.

This result are different from those of the studies performed by Talamini, G et al. (35)and Ocampo C et al. (36). Talamini, G. found thata pleural effusion and/or pulmonary infiltrates during the first 24 hours may be associated with severe course of the disease and organ failure. Ocampo C. et al. found that pleural effusion can predict with a great accuracy severe acute pancreatitis. The different result of our study may be explained that pleural effusion was detected by chest roentgenogram rather than ultrasonography as was performed in Ocampo's study.

Age, total calcium, total bilirubin and amylase levels showed little statistical significance in this study.

In the current study, in group 1, the mean **age** was 44 ± 16 years old. While in group 2, the mean age was 48 ± 12 years old. The *P* value was 0.6 which is statistically insignificant. This means that age is of no value in the prediction of severe acute pancreatitis in this study.

Several studies have concluded that older age is a predictor of a worse prognosis, although the age cutoff was varied from 55 to 75 years in different reports. In an illustrative study by Frey CF et al. (37), patients older than 75 years had more than a 15-fold greater chance of dying within two weeks and a more than 22-fold greater chance of dying within 91 days compared with patients aged 35 years or younger. Gardner, T.B. et al. (38) found that age more than 79 years old is an independent predictor of severe acute pancreatitis. Age was irrelevant in this study and this can be explained by the heterogeneity of the cohort study.

Serum amylase level mean value in group 1 was 653.1 ± 368.9 U/L while in group 2 was 1054.2 ± 714.9 U/Land P value of 0.11 which is statistically insignificant. Serum amylase rises within 6 to 12 hours of the onset of acute pancreatitis. Amylase has a short half-life of approximately 10 hours and in uncomplicated attacks returns to normal within three to five days. Serum amylase elevation of greater than three times the upper limit of normal has a sensitivity for the diagnosis of acute pancreatitis of 67 to 83 % and a specificity of 85 to 98 %(31). However, elevations in serum amylase to more than three times the upper limit of normal may not be seen in approximately 20 % of patients with alcoholic pancreatitis due to the inability of the parenchyma to produce amylase, and in 50 % of patients with hypertriglyceridemia-associated pancreatitis as triglycerides interfere with the amylase assay(39).

This study results are supported by the study of Manes, G. et al who found that serum lipase and amylase levels were not useful in either detecting the etiology nor predicting the severity of acute pancreatitis (34).

Total calcium level in group 1 was 2.07±0.32 while in group 2 was 2.38±1.04 with a P value of 0.3 which is statistically insignificant.

Although, Maher M. et.al found in a study performed on 149 patients that total calcium level has a P value of 0.67 and is statistically insignificant as a predictor of severity(7), but Gutierrez-Jimenez A. A. et al found that total calcium is a powerful predictor of severity in the first 24 hours(8). There are differences in the population numbers between the two studies and this may explain the varying results.

Also total bilirubin showed P value of 0.3 which is statistically insignificant as a predictor of severity.

Maher, M. et.al found that total bilirubin level has a P value of 0.09 and is statistically inferior as a predictor of severity(7). However, Chan T. et al found that in gallstone pancreatitis, a serum total bilirubin level 4 mg/dL or greater on hospital Day 2 predicts persisting common bile duct stones with enough specificity to serve as a practical guideline for ERCP while minimizing unnecessary procedures(40). The result of our study can be explained by the heterogeneity of the cohort population and that bilirubin levels was obtained at admission.

Body temperature, heart rate and blood pressure were obtained from the patients of this study. Body temperature showed no statistical significance with P value of 0.27. On the other hand, heart rate and blood pressure showed good statistical discrepancy between the two groups, the heart rate mean±SD of 75.714 beats per second on the first group and 99±6.81 beats per minutes in the second group with P value of <0.001. The increased heart rate in the second group is due to physiological compensation to the third space fluid loss.

Systolic blood pressure mean±SD in the first group was 102.5±8.49 mm Hg and in the second group was 85.83±5.85 mm Hg with P value of <0.001. The diastolic blood pressure mean±SD was 62.86±5.08 mm Hg in the first group and 49.17±8.61 mm Hg in the second group with p value of <0.001. The lower blood pressure in the second group was due to third space fluid loss and shock due to the severe inflammatory process.

Conclusion

In conclusion, Blood glucose level, AST and platelets count showed the highest AUC, sensitivity, specificity, PPV, NPV and accuracy among other proposed predictors. Although other proposed predictors showed lower results than the

above mentioned predictors, they still have very significant NPV and can be used to rule out severe acute pancreatitis.

References

1. Papachristou GI, Clermont G, Sharma A, Yadav D, Whitcomb DC. Risk and markers of severe acute pancreatitis. Gastroenterology clinics of North America. 2007;36(2):277-96, viii.
2. Swaroop VS, Chari ST, Clain JE. Severe acute pancreatitis. JAMA : the journal of the American Medical Association. 2004;291(23):2865-8.
3. Isenmann R, Beger HG. Natural history of acute pancreatitis and the role of infection. Bailliere's best practice & research Clinical gastroenterology. 1999;13(2):291-301.
4. Whitcomb DC. Clinical practice. Acute pancreatitis. The New England journal of medicine. 2006;354(20):2142-50.
5. Robert JH, Frossard JL, Mermillod B, Soravia C, Mensi N, Roth M, et al. Early prediction of acute pancreatitis: prospective study comparing computed tomography scans, Ranson, Glascow, Acute Physiology and Chronic Health Evaluation II scores, and various serum markers. World journal of surgery. 2002;26(5):612-9.
6. Windsor JA. Search for prognostic markers for acute pancreatitis. Lancet. 2000;355(9219):1924-5.
7. Maher MM, Dessouky BAM. Simplified early predictors of severe acute pancreatitis: a prospective study. Gastroenterology Research. 2010;3(1):25-31.
8. Gutierrez-Jimenez AA, Castro-Jimenez E, Lagunes-Cordoba R. [Total serum calcium and corrected calcium as severity predictors in acute pancreatitis]. Revista de gastroenterologia de Mexico. 2014;79(1):13-21.
9. Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, et al. Classification of acute pancreatitis--2012: revision of the Atlanta classification and definitions by international consensus. Gut. 2013;62(1):102-11.
10. Marshall JC, Cook DJ, Christou NV, Bernard GR, Sprung CL, Sibbald WJ. Multiple organ dysfunction score: a reliable descriptor of a complex clinical outcome. Critical care medicine. 1995;23(10):1638-52.
11. Sarles H. Revised classification of pancreatitis--Marseille 1984. Digestive diseases and sciences. 1985;30(6):573-4.
12. Peery AF, Dellon ES, Lund J, Crockett SD, McGowan CE, Bulsiewicz WJ, et al. Burden of gastrointestinal disease in the United States: 2012 update. Gastroenterology. 2012;143(5):1179-87 e1-3.
13. Fagenholz PJ, Castillo CF, Harris NS, Pelletier AJ, Camargo CA, Jr. Increasing United States hospital admissions for acute pancreatitis, 1988-2003. Annals of epidemiology. 2007;17(7):491-7.
14. Fisher JM, Gardner TB. The "golden hours" of management in acute pancreatitis. The American journal of gastroenterology. 2012;107(8):1146-50.
15. Frossard JL, Hadengue A, Pastor CM. New serum markers for the detection of severe acute pancreatitis in humans. American journal of respiratory and critical care medicine. 2001;164(1):162-70.
16. Remes-Troche JM, Duarte-Rojo A, Morales G, Robles-Diaz G. Hemoconcentration is a poor predictor of severity in acute pancreatitis. World journal of gastroenterology : WJG. 2005;11(44):7018-23.
17. Lin G, Halevy A, Girtler O, Gold-Deutch R, Zisman A, Scapa E. The role of endoscopic retrograde cholangiopancreatography in management of patients recovering from acute biliary pancreatitis in the laparoscopic era. Surgical endoscopy. 1997;11(4):371-5.
18. Burtis CA, Ashwood ER, Bruns DE, Tietz NW. Tietz textbook of clinical chemistry and molecular diagnostics. 5th ed. St. Louis, Mo.: Saunders; 2013. xviii, 2,238 p. p.
19. Zhang XY, Lin ZQ, Xue P, Xia Q. [Clinical study on different admission serum glucose levels in patients with severe acute pancreatitis]. Sichuan da xue xue bao Yi xue ban = Journal of Sichuan University Medical science edition. 2013;44(6):974-7, 86.
20. Muddana V, Whitcomb DC, Khalid A, Slivka A, Papachristou GI. Elevated serum creatinine as a marker of pancreatic necrosis in acute pancreatitis. The American journal of gastroenterology. 2009;104(1):164-70.
21. Papachristou GI, Whitcomb DC. Predictors of severity and necrosis in acute pancreatitis. Gastroenterology clinics of North America. 2004;33(4):871-90.
22. Blum T, Maisonneuve P, Lowenfels AB, Lankisch PG. Fatal outcome in acute pancreatitis: its occurrence and early prediction. Pancreatology : official journal of the International Association of Pancreatology. 2001;1(3):237-41.
23. Frank B, Gottlieb K. Amylase normal, lipase elevated: is it pancreatitis? A case series and review of the literature. The American journal of gastroenterology. 1999;94(2):463-9.
24. Wu BU, Johannes RS, Sun X, Conwell DL, Banks PA. Early changes in blood urea nitrogen predict

mortality in acute pancreatitis. Gastroenterology. 2009;137(1):129-35.

25. Fujimura Y, Hirota M, Ichihara A, Takamori H, Baba H. Platelet count as a sensitive and convenient parameter for assessing the prognosis in acute pancreatitis. Pancreas. 2008;37(2):225-7.

26. Bonfrate L, Wang DQ, Garruti G, Portincasa P. Obesity and the risk and prognosis of gallstone disease and pancreatitis. Best practice & research Clinical gastroenterology. 2014;28(4):623-35.

27. Shin KY, Lee WS, Chung DW, Heo J, Jung MK, Tak WY, et al. Influence of obesity on the severity and clinical outcome of acute pancreatitis. Gut and liver. 2011;5(3):335-9.

28. Wilson C, Heads A, Shenkin A, Imrie CW. C-reactive protein, antiproteases and complement factors as objective markers of severity in acute pancreatitis. The British journal of surgery. 1989;76(2):177-81.

29. Ke L, Tong ZH, Li WQ, Wu C, Li N, Windsor JA, et al. Predictors of critical acute pancreatitis: a prospective cohort study. Medicine. 2014;93(21):e108.

30. Lankisch PG, Mahlke R, Blum T, Bruns A, Bruns D, Maisonneuve P, et al. Hemoconcentration: an early marker of severe and/or necrotizing pancreatitis? A critical appraisal. The American journal of gastroenterology. 2001;96(7):2081-5.

31. Yadav D, Agarwal N, Pitchumoni CS. A critical evaluation of laboratory tests in acute pancreatitis. The American journal of gastroenterology. 2002;97(6):1309-18.

32. Coffey MJ, Nightingale S, Ooi CY. Serum lipase as an early predictor of severity in pediatric acute pancreatitis. Journal of pediatric gastroenterology and nutrition. 2013;56(6):602-8.

33. Gwozdz GP, Steinberg WM, Werner M, Henry JP, Pauley C. Comparative evaluation of the diagnosis of acute pancreatitis based on serum and urine enzyme assays. Clinica chimica acta; international journal of clinical chemistry. 1990;187(3):243-54.

34. Manes G, Rabitti PG, Laccetti M, Pacelli L, Carraturo I, Uomo G. Early prediction of aetiology and severity of acute pancreatitis by serum amylase and lipase assays. Minerva gastroenterologica e dietologica. 1995;41(3):211-5.

35. Talamini G, Uomo G, Pezzilli R, Rabitti PG, Billi P, Bassi C, et al. Serum creatinine and chest radiographs in the early assessment of acute pancreatitis. American journal of surgery. 1999;177(1):7-14.

36. Ocampo C, Silva W, Zandalanzini H. "Pleureal Effusion is Superior to Multiple Factor Scoring System in predicting Acute Pancreatitis outcome". Acta Gastroenterol Latinoam(in Spanish). 2008; Mar: 38(1): 34-42.

37. Frey CF, Zhou H, Harvey DJ, White RH. The incidence and case-fatality rates of acute biliary, alcoholic, and idiopathic pancreatitis in California, 1994-2001. Pancreas. 2006;33(4):336-44.

38. Gardner TB, Vege SS, Chari ST, Pearson RK, Clain JE, Topazian MD, et al. The effect of age on hospital outcomes in severe acute pancreatitis. Pancreatology : official journal of the International Association of Pancreatology. 2008;8(3):265-70.

39. Fortson MR, Freedman SN, Webster PD, 3rd. Clinical assessment of hyperlipidemic pancreatitis. The American journal of gastroenterology. 1995;90(12):2134-9.

40. Chan T, Yaghoubian A, Rosing D, Lee E, Lewis RJ, Stabile BE, et al. Total bilirubin is a useful predictor of persisting common bile duct stone in gallstone pancreatitis. The American surgeon. 2008; 4(10):977-80.