Original Article

Serum D-dimer is a Predictor of Severity and Outcome of Acute Pancreatitis

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Abstract:

Background: *Acute pancreatitis (AP) is characterized by a spectrum of symptoms, ranging from a local inflammatory process to the more severe form (acute necrotizing pancreatitis) which is associated with a systemic inflammatory response. The overall mortality rate of AP is between 5% and 15%, reaching 30 % in severe acute pancreatitis (SAP). Early optimized care may improve prognosis in patients with the most severe forms but it remains a challenge to identify these poor prognosis cases specially in the first 48 hours. The objective of our study is to evaluate the efficacy of serum D-dimer in the prediction of severity and outcome of acute pancreatitis.*

Methods: *This prospective and observational study was conducted in the Department of Gastrointestinal, Hepatobiliary and Pancreatic Disorders (GHPD), BIRDEM General Hospital, Dhaka, Bangladesh from January, 2016 to September, 2017. Patients with acute pancreatitis admitted to Department of GHPD of BIRDEM General Hospital, Dhaka, were included in this study. Purposive type of non probability sampling technique was applied to enroll the patients. A predesigned structured questionnaire was used for recording the necessary information. Patients admitted with abdominal pain and fulfilling the diagnostic criteria of acute pancreatitis by clinical history, physical examination, biochemical tests and different imaging modalities and patients aged more than 18 years were included in this study. The patients were followed up on day 1, day 3 of admission and on the day before discharge.*

Results: *Total 87 patients with acute pancreatitis, who fulfilled the inclusion criteria, were included in this study. This study found that 53(61.0%) had mild acute pancreatitis, 27(31.0%) patients had moderately severe acute pancreatitis and 7(8.0%) patients had severe acute pancreatitis. The mean serum D-dimer at day 1 of patients with mild disease was 2.31± 1.82(mean±SD) µg/ml, in patients with moderately severe disease was 4.67± 2.02(mean±SD) µg/ml and in severe acute pancreatitis it was 10.11±3.11 (mean±SD) µg/ml. The difference among the groups were statistically significant (p<0.001). The mean serum D-dimer at day 3 of patients with mild disease was 0.8±0.51 (mean±SD) µg/ml, in patients with moderately severe disease was 1.86±2.22 (mean± SD) µg/ml and in severe acute pancreatitis it was 3.62±1.9 (mean±SD) µg/ml. The difference among the groups were statistically significant (p<0.001). Thus serum D-dimer could predict disease severity early in the course of disease successfully. In the present study 55(63.2%) patients did not develop any kind of complications and serum D-dimer level at day 1 and day 3 were 2.4±1.73 and 0.81±0.49 respectively. On the other hand 32 (36.8%) patients developed complications and serum D-dimer level at day 1 and day 3 were 5.86±3.5 and 2.31±2.3 respectively. The difference among the groups were statistically significant (p<0.001).That reveals serum D-dimer is a predictor of outcome of acute pancreatitis. Sensitivity, specificity and accuracy was 77.8%, 76.5% and 77.0% respectively at day 1 (cut off value e"3.3 µg/ml) and it was 73.5%, 77.4% and 75.9% respectively at day 3 (cut off value e"1.05 µg/ml) in prediction outcome of AP.*

Conclusion: *The difference of serum D-dimer levels between mild, moderately severe and severe acute pancreatitis was statistically significant and it was also higher in patients who developed complications following acute pancreatitis than those without complications. This simple, feasible and reproducible marker can be used in clinical practice to improve the early management of acute pancreatitis.*

Key words: *Serum D-dimer, predictor,acute pancreatitis.*

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Introduction

Acute pancreatitis is best defined clinically by a patient presenting with two of the following three criteria[1]: (1) symptoms (epigastric pain) consistent with pancreatitis, (2) a serum amylase or lipase greater than three times the upper limit of normal and (3) radiologic imaging consistent with pancreatitis, usually using computed tomography (CT) or magnetic resonance imaging (MRI).[2]

Up to 12-25% of the patient developed severe acute pancreatitis (SAP), which has a mortality rate of 8-25%.[3] Mortality in SAP occurs either early, due to an overwhelming inflammatory reaction or late, owing to sepsis related complications such as septic shock and major bleeding primarily arising from infected pancreatic necrosis.

About 3% of all cases of abdominal pain admitted to hospital are acute pancreatitis cases.[4] The incidence of acute pancreatitis appears to be increasing.[5] The overall mortality rate of AP is between 5% and 15%, reaching 30 % in severe AP[6]: these patients develop extensive pancreatic inflammation and necrosis, a systemic inflammatory response syndrome, and multiple organ failure. Early optimized care may improve prognosis in patients with the most severe forms but it remains a challenge to identify these poor prognosis cases specially in the first 48 hours. The validated severity scoring systems require 48 hours of observation which may miss a potentially valuable early therapeutic window.[7]

About 80% of all cases are mild and have favorable outcome. Of the rest 20% of patient with severe disease, almost all (98%) die within the first week, usually from multiorgan failure. After this time the majority of deaths result from sepsis, specially that complicating infected necrosis. On admission it is possible to predict patients at risk of this complication.[4]

Once the diagnosis of acute pancreatitis is established, the patients are classified based on disease severity. The Atlanta Criteria revision of 2012[1] classifies severity as mild, moderately severe and severe. Mild acute pancreatitis the commonest form has no organ failure, no local or systemic complications and usually resolves within the first week. Moderately severe acute pancreatitis is defined by transient organ failure (lasting <48 hours) and/or local or systemic complications without persistent organ failure. Severe acute pancreatitis was defined by persistent single or multiple organ failure lasting for >48 hours. Local complications include peripancreatic fluid collections, pancreatic and peripancreatic necrosis (sterile or infected), pseudocyst and walled-off necrosis (sterile or infected).[2]

In acute pancreatitis, early assessment of the patient which can lead to an accurate prediction of the severity is useful for several reasons. The first well established step is the need to categorize patients at risk for complications for appropriate stratification in clinical trial. Furthermore it is important to identify the patients who are at risk for developing complications in order to be able to initiate effective management before those complications developed [8].

The lack of accurate predictors of disease severity makes such categorization difficult. Several biochemical parameters, contrast enhanced computed tomography and multiple clinico-biochemical scores have been used to assess the severity of acute pancreatitis. An ideal prognostic method should be simple, cheap, routinely available and highly accurate. Such a method is however not yet available.

The pathogenesis of organ dysfunction in AP leads to systemic inflammation, cytokine activation and sequestration, hyper coagulation and consequently micro vascular thrombosis. Pro-inflammatory cytokines induce expression of tissue factor, a glycoprotein that activates the blood coagulation extrinsic pathway, on mononuclear and endothelial cells, thereby linking inflammation and hypercoagulation[9]. Therefore, markers of coagulation including serum D-dimer, usually increase in AP and platelet count, prothrombin time or antithrombin III decrease. A few studies have evaluated the value of coagulation markers in the prediction of pancreatitis severity and outcomes including D-dimer, but a definitive predictive biomarker have not yet to be established.[10]

D-dimer is a fibrin degradation product (or FDP), a small protein fragment present in the blood after a blood clot is degraded by fibrinolysis. It is so named because it contains two cross linked D fragments of the fibrin protein.[11]Coagulative derangements and disturbance of the microcirculations are known to occur in the early phase of AP and are related to its severity.[12] Coagulative disorders in these patients may range from scattered

intravascular thrombosis to severe disseminated intravascular thrombosis (DIC).[13] In previous studies, some hemostatic system related parameters have been shown to be potential predictors of acute pancreatitis severity and outcome.[10,12,14] D-dimer which is mostly used as an effective diagnostic tool to rule out deep vein thrombosis (DVP) as well as pulmonary embolism (PE) [15,16] has been reported to have great predictive power in the early phase of AP.

In the present study, we aim to identify the association between D-dimer level in the first few days of AP and several clinical variables. Furthermore, the accuracy of the D-dimer level for the prediction and correlation between the D-dimer level and severity, outcome and other common severity markers were also studied.

This study also used to evaluate a simple and easily accessible D-dimer testing for the early prediction of severity and outcome of AP. The primary objective was to evaluate serum D-dimers on day 1 of pain onset as an early predictor of severity defined by using the AP Atlanta criteria. The secondary objective was to evaluate serum D-dimers on day 3 of pain onset as an early predictor of severity, complications and outcome to determine an optimal D-dimer threshold value and compare the D-dimer assay with validated AP severity criteria (Glasgow score, BISAP score, Ranson score and CRP).

Serum D-dimer has been introduced as an early marker of severe inflammation and it may play a vital role in predicting the severity of acute pancreatitis. Several studies have been conducted to establish its role in the early prediction of severity of acute pancreatitis. But no such study is done in our country till now. This study aims at evaluating the role of serum D-dimer in the prediction of severity and outcome of acute pancreatitis. This study will help in early recognition of severity and outcome of acute pancreatitis.

The objective of our study is to evaluate the efficacy of serum D-dimer in the prediction of severity and outcome of acute pancreatitis, to compare serum D-dimer levels with the Glasgow score, Ranson score and BISAP score as a predictor of severity and outcome in acute pancreatitis and to compare serum D-dimer levels with CRP levels as a predictor of severity and outcome in acute pancreatitis.

Methods

This prospective and observational study was conducted in the Department of Gastrointestinal, Hepatobiliary and Pancreatic Disorders (GHPD), BIRDEM General Hospital, Dhaka, Bangladesh from January, 2016 to September, 2017.

Patients with acute pancreatitis admitted to Department of Gastrointestinal Hepatobiliary and Pancreatic Disorders (GHPD) of BIRDEM General Hospital, Dhaka, were included in this study.

Purposive type of non probability sampling technique was applied to enroll the patients.

Patients were selected from BIRDEM General Hospital. A predesigned structured questionnaire was used for recording the necessary information.

Inclusion criteria: Patients admitted with abdominal pain and fulfilling the diagnostic criteria of acute pancreatitis by clinical history, physical examination, biochemical tests and different imaging modalities and patients aged more than 18 years were included in this study.

Exclusion criteria: Patients attending after 24 hours of onset of abdominal pain, having chronic pancreatitis serious co-morbid conditions like COPD and heart failure, pulmonary embolism and/or Deep vein thrombosis and patients unwilling to give voluntary consent to participate in the study were excluded from this study.

Demographic and clinical variables were age, sex, BMI, duration of hospital stay, abdominal pain, severity of pain, radiation of pain, fever, co-morbid illness, smoking, alcohol, drug history, family history, history of previous attack, vital parameters and GCS score.

Laboratory variables were hemoglobin level, WBC count, serum electrolyte, serum calcium, random blood sugar, HbA1c, blood urea, BUN, serum creatinine, liver function test, serum amylase, serum lipase, fasting lipid profile, serum LDH, ABG, CA 19.9, serum D-dimer, USG, CT scan findings.

Sample was selected through non-probability sampling method from patients who present with acute abdominal pain. Informed written consent was taken from each patient before enrollment. History of each patient was taken and was recorded. A questionnaire was filled up by the investigator which contained information regarding past history of abdominal pain, alcohol intake, drug history, family history of pancreatitis and other co-morbidities.

To detect etiology of acute pancreatitis, liver function test, fasting lipid profile, USG of abdomen were done

in all cases. Physical examination was done systematically by the investigator on the day of admission and on subsequent visit.

Baseline investigations including serum amylase, serum lipase and serum D-dimer were done in all patients on admission or within 24 hours. USG of whole abdomen was done for every patients. CT scan of abdomen were done where applicable.

Glasgow score, Ranson score and BISAP score was calculated using the data available after admission.

Attacks of acute pancreatitis were classified as mild, moderately severe and severe according to Revised Atlanta Criteria and with the help of modified Marshall scoring system for organ failure.

Every patient was follow up regularly for identification of organ failure or any other complication.

All patients with questionable diagnosis of other possible abdominal conditions and incomplete data collections were excluded in this study. All patients with clinical presentations suggestive of chronic pancreatitis such as pancreatic duct dilatation, calcifications and malabsorption were excluded.

The patients were followed up on day 1, day 3 of admission and on the day before discharge.

Operational definitions

Acute pancreatitis: Acute pancreatitis is best defined clinically by a patient presenting with two of the following three critera[1]: (1) symptoms (epigastric pain) consistent with pancreatitis, (2) serum amylase or lipase greater than three times the upper limit of normal, and (3) radiologic imaging consistent with pancreatitis, usually using computed tomography (CT) or magnetic resonance imaging (MRI) [2].

Biliary pancreatitis: Patient with diagnosis of acute pancreatitis with no history of alcohol abuse and imaging techniques showing gall stones or biliary sludge [17].Biliary pancreatitis was also considered if serum ALT is > 150 U/L with a specificity of 96% [2].

Hypertriglyceridaemia induced pancreatitis: Fasting serum Triglyceride level within 24 hours of admission >1000 mg/dl was considered as hyper triglyceridaemia induced acute pancreatitis [18].

Alcoholic pancreatitis: Acute pancreatitis in a patient with heavy alcohol consumption (>50 gm/day) for more than 5 years was considered as acute alcoholic pancreatitis[18].

Severity of pancreatitis: Severity will be assessed by Atlanta criteria revision of 2012 for severity of acute pancreatitis.The Atlanta criteria revision of 2012 classifies severity as mild, moderately severe, or severe. Mild acute pancreatitis the commonest form, has no organ failure, no local or systemic complications, and usually resolves within the first week. Moderately severe acute pancreatitis is defined by transient organ failure (lasting <48 hours) and/ or local/systemic complications. Severe acute pancreatitis was defined by presence of persistent single or multiple organ failure lasting for >48 hours [1] .Local complications include peripancreatic fluid collections, pancreatic and peripancreatic necrosis (sterile or infected), pseudocyst, and walled-off necrosis.

Outcome of acute pancreatitis: Outcome of acute pancreatitis was categorized into acute pancreatitis without any complication, acute pancreatitis with complication and death from sequel of acute pancreatitis.

Organ failure: It was defined according to the Modified Marshall Scoring System, a universally applicable scoring system for identifying organ failure.

Modified Marshall Scoring System[19]

Organ system	Score				
	0	1	2	3	4
Respiratory PaO2/ FiO2	>400	301-400	201-300	101-200	<101
Renal	<134	134-169	170-310	311-439	>439
S. creatinine µmol/L (mg/dl)	(<1.51)	1.51-1.91	1.92-3.50	3.51-4.96	>4.96
Cardiovascular	>90	<90	<90	<90	<90
systolic BP (mm Hg)		responsive to fluid resuscitation	not responsive to fluid resuscitation	pH<7.3	pH<7.2

- a score of ≥2 in any one organ system defines "organ failure"
- serum creatinine : 88.4 micro mol/L = 1 mg/dl

Data were collected in a pre-designed data-sheet which contains questionnaire, clinical findings and biochemical and imaging findings.

Statistical analyses were carried out by using the Statistical Package for Social Sciences version 16.0 for Windows (SPSS Inc, Chicago, Illinois, USA). Continuous variables were expressed as mean, standard deviation, and categorical variables as frequencies and percentages. The differences between groups were analyzed by unpaired t-test, chi-square (χ^2) test, and ANOVA test. Correlation between variables was measured by Spearman correlation coefficient test. A p-value <0.05 was considered as significant.

Ethical consideration

Prior to the commencement of this study, the research protocol was approved by the local ethical committee. The aims and objective of the study along with its procedure, alternative diagnostic methods, risk and benefits were explained to the patients in easily understandable local language and then informed consent was taken from each patient. It was assured that all records would be kept confidential and the procedure would be helpful for both the physician and patients in making rational approach regarding management of the case.

Results

A prospective and observational study was carried out to evaluate the role of serum D-dimer in predicting severity and outcome of acute pancreatitis. Total 87 patients with acute pancreatitis, who fulfilled the inclusion criteria, were included in this study. The result of the study was presented in following tables and figures.

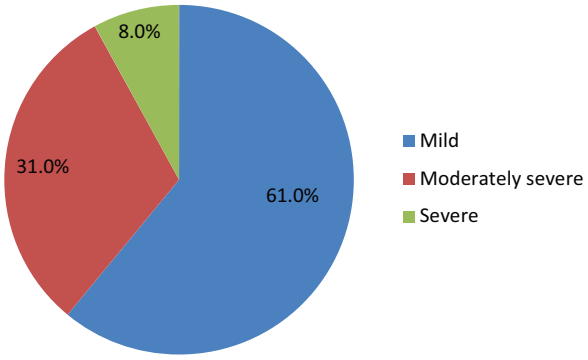

Figure 1 Distribution of patients according to severity of acute pancreatitis based on Revised Atlanta Criteria (n=87)

Table I Demographic, clinical and biochemical characteristics of the study population (n=87)

Parameters	Result
Age (years)	51.5±15.6
Gender	
Male	51(58.6)
Female	36(41.4)
Contributing factor	
Alcohol	6(6.9)
BMI (m^2/kg)	24.9±5.3
Clinical features	
Abdominal pain	87(100.0)
Nausea and / or vomiting	82(94.3)
Fever	8(9.2)
Co-morbidity	
DM	58(66.7)
HTN	3(3.4)
Multiple	13(14.9)
Serum amylase(U/L)	603[103-9395]
Serum lipase(U/L)	14000[225-17900]
Blood sugar (Fasting) mmol/L	11.1±3.7
HbA1c(%)	7.8±2.0
Duration of hospital stay (days)	6.5±5.2
HCT (%)	41.7±6.1
Blood urea nitrogen (mg/dl)	31.9±18.2
CRP (mg/dl)	110.2±73.9
D-dimer day 1 (µg/ml)	3.7±2.9
D-dimer day 3 (µg/ml)	1.4±1.6

Values are expressed as mean±SD. Values within the bracket are expressed as percentage. Value of serum amylase and serum lipase expressed as median and range.

Table II Association of serum D-dimer with severity of acute pancreatitis (based on Revised Atlanta Criteria (n=87)

Severity of acute pancreatitis	n(%)	Serum D-dimer Day 1 (µg/ml) (Mean±SD)	Serum D-dimer Day 3 (µg/ml) (Mean±SD)
Mild	53(61.0)	2.31±1.82	0.80±0.51
Moderately severe	27(31.0)	4.67±2.02	1.86±2.22
Severe	7(8.0)	10.11±3.11	3.62±1.90
p value		<0.001	<0.001

ANOVA test was done to measure the level of significance

Table III Association between serum D-dimer and outcome of acute pancreatitis (n=87)

Outcome of acute pancreatitis	n (%)	Serum D-imer Day 1 (µg/ml) (Mean±SD)	Serum D-dimer Day 3 (µg/ml) (Mean±SD)
Developed no complication	55(63.2)	2.40±1.73	0.81±0.49
Developed complication	32(36.8)	5.86±3.35	2.31±2.30
p value		<0.001	<0.001

Unpaired t test was done to measure the level of significance

Table IV Comparison of coagulation profile of the studied subjects of acute pancreatitis (n=87)

Characteristics	Mild (n-53) (mean±sd)	Moderate (n-27)(mean±sd)	Severe (n-7)(mean±sd)	p[a] value
PT day 1 (sec)	14.0±1.4	15.1±1.4	15.9±0.4	<0.001
PT day 3 (sec)	13.2±1.0	13.6±0.7	14.0±0.4	0.039
APTT day 1 (sec)	27.1±1.6	28.5±1.9	26.8±2.0	0.002
APTT day 3 (sec)	26.8±0.8	28.0±2.5	27.2±1.6	0.008
Fibrinogen day 1 (mg/dl)	301±78.8	299.9±55.6	225.1±25.1	0.025
Fibrinogen day 3 (mg/dl)	296.8±47.5	303.0±51.1	237.0±94.0	0.014

[a] ANOVA test was done to measure the level of significance

Table V Area under curve (AUC) of D-dimer day 1 and D-dimer day 3 in prediction of severity of acute pancreatitis

Test Variable(s)	AUC	p value	95% Confidence Interval	
			Lower Bound	Upper Bound
D-dimer at Day 1	0.867	<0.001	0.785	0.948
D-dimer at Day 3	0.838	<0.001	0.754	0.922

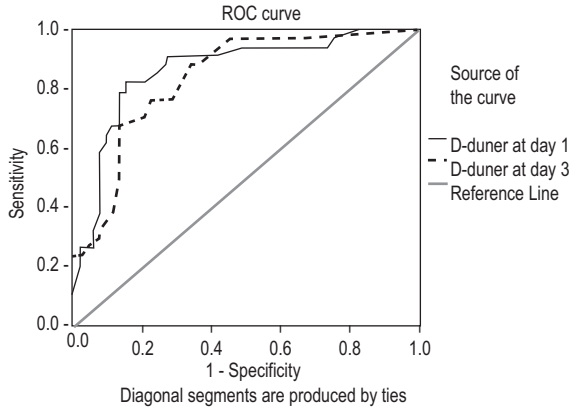

Figure 2 ROC curve of D-dimer day 1 and D-dimer day 3 in prediction of severity of acute pancreatitis. AUC of D-dimer at day 1 was 0.867 and at day 3 was 0.838

Table VI Sensitivity and specificity of D-dimer at day 1 at different cut off values in prediction of severity of acute pancreatitis (n=87)

Cut off (µg/ml) (≥, Greater than or equal to)	Sensitivity %	Specificity %
2.65	84.4	67.3
3.15	81.3	76.4
3.30	81.3	81.8
3.45	78.1	81.8
4.05	75.0	85.5

Table VII Sensitivity and specificity of D-dimer at day 3 at different cut off values in prediction of severity of acute pancreatitis (n=87)

Cut off (µg/ml) (≥, Greater than or equal to)	Sensitivity%	Specificity%
0.85	85.3	67.9
0.95	76.5	71.7
1.05	76.7	77.3
1.15	70.6	79.2
1.25	67.6	86.8

Table VIII Diagnostic usefulness of D-dimer value on day 1 and day 3 in prediction of severity of acute pancreatitis (n=87)

Diagnosticmethod	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Diagnostic accuracy (%)
D-dimer Day 1(cut off value ≥3.3 µg/ml)	81.3	81.8	72.2	88.2	87.7
D-dimer Day 3(cut off value ≥1.05µg/ml)	76.7	77.3	76.7	77.3	82.7

PPV –Positive predictive value, NPV –Negative predictive value

Table IX Performance test of serum D-dimer at day 1 in predicting outcome of acute pancreatitis (n=87)

Serum D-dimer (µg/ml)	Outcome		Total	P value
	With complication	Without complication		
D-dimer ≥3.3	28	12	40	<0.001
D-dimer <3.3	8	39	47	
Total	32	55	87	

Chi-square (X^2) test was done to measure the level of significance

Table X Performance test of serum D-dimer at day 3 in predicting outcome of acute pancreatitis (n=87)

Serum D-dimer (µg/ml)	Outcome		Total	p[a] value
	With complication	Without complication		
D-dimer ≥1.05	25	12	37	<0.001
D-dimer <1.05	9	41	50	
Total	32	55	87	

[a]Chi-square (X^2) test was done to measure the level of significance

Table XI Diagnostic usefulness of D-dimer value on day 1 and day 3 for prediction of outcome of acute pancreatitis (n=87)

Diagnosticmethod	Sensitivity (%)	Specificity (%)	PPV (%)	NPV(%)	Diagnostic accuracy (%)
D-dimer Day 1(cut off value ≥3.3)	77.8	76.5	70.0	83.0	77.0
D-dimer Day 3(cut off value ≥1.05)	73.5	77.4	67.6	82.0	75.9

PPV –Positive predictive value, NPV –Negative predictive value

Table XII D-dimer day 1, D-dimer day 3, Glasgow score, BISAP score, Ranson score and CRP in patients with acute pancreatitis according to severity of acute pancreatitis based on Revised Atlanta Criteria (n=87)

Marker	Mild	Moderately severe	Severe	p[a] value
D-dimer at day 1	2.32±1.83	4.67±2.02	10.11±3.11	<0.001
D-dimer at day 3	0.81±0.52	1.87±2.23	3.63±1.90	<0.001
Glasgow score	1.68±1.38	3.78±1.72	4.43±1.27	<0.001
BISAP	0.85±0.89	2.19±0.96	3.43±0.53	<0.001
Ranson score	1.60±1.29	1.89±1.01	2.43±0.53	0.175
CRP	95.58±71.44	127.00±65.26	155.86±99.60	0.044

[a]ANOVA test was done to measure the level of significance

Table XIII Comparison of D-dimer day 1, D-dimer day 3, Glasgow score, BISAP score, Ranson score and CRP level in patients with acute pancreatitis without complication and with complication (n=87)

Marker	Acute pancreatitis without complication	Acute pancreatitiswith complication	p[a] value
D-dimer at day 1	2.40±1.73	5.86±3.35	<0.001
D-dimer at day 3	0.81±0.49	2.31±2.30	<0.001
Glasgow score	1.85±1.53	3.75±1.72	<0.001
BISAP score	0.91±0.89	2.44±1.11	<0.001
Ranson score	1.65±1.35	1.93±0.80	0.284
CRP	98.35±71.46	130.53±74.59	0.049

[a] ANOVA test was done to measure the level of significance

Table XIV Correlation of serum D-dimer with Glasgow, Ranson, BISAP score and CRP

Marker	r value	p value
Serum D-dimer	1.0	<0.001
Glasgow score	0.573	<0.001
Ranson score	0.646	<0.001
BISAP score	0.254	0.017
CRP	0.329	0.002

Spearman test was done to measure the level of significance

Discussion

The coagulative system disturbance has long been thought to be implicated in the pathogenesis of the systemic and local complications of acute pancreatitis[10]. As for D-dimer, which is a fibrin degradation product, there have been very few studies so far about its value in the prediction of severity during acute pancreatitis(AP) .This prospective observational study was carried out to evaluate the role of serum D-dimer in predicting severity and outcome of acute pancreatitis. Total 87 patients with acute pancreatitis, who fulfilled the inclusion criteria, were included in this study.

In this study 58(66.7%) patients were diabetic and this can be explained by inclusion of patients from a tertiary level diabetic hospital. Out of 87 cases, 6(6.9%) were alcoholic and mean BMI was 24.9±5.3 (table I).

In the studied subject mean hematocrit on admission was 41.7±6.1, mean blood urea nitrogen was 31.9±18.2, mean HbA_{1c} was 7.8±2.0 and average duration of hospital stay was 6.5±5.2 days (table I).

Gomercic et al.[19] showed that the duration of hospitalization was higher for complicated AP (15.2 vs 7.5 days, P = 0.002).

This study found that majority of the cases etiology could not be found 40(46%). Among the cases, 20(23%) were gall stone pancreatitis, 12(13.8%) cases hyper triglyceridaemia, 6(6.9%) cases were due to alcohol, 8(9.2%) cases were due to pancreatic malignancy.

This study found that according to revised Atlanta criteria, 53(61.0%) had mild acute pancreatitis, 27(31.0%) patients had moderately severe acute pancreatitis and 7(8.0%) patients had severe acute pancreatitis (figure 1). In their study Cho et al.[20] found 13% cases as severe acute pancreatitis, 8% cases as moderately severe and 79% cases as mild acute pancreatitis which is consistent with the present study.

The mean serum D-dimer at day 1 of patients with mild disease was 2.31± 1.82(mean±SD) µg/ml, in patients with moderately severe disease was 4.67± 2.02(mean±SD) µg/ml and in severe acute pancreatitis it was 10.11±3.11(mean±SD) µg/ml. The difference among the groups were statistically significant (Table II; p<0.001).The mean serum D-dimer at day 3 of patients with mild disease was 0.8±0.51 (mean±SD) µg/ml, in patients with moderately severe disease was 1.86±2.22 (mean± SD) µg/ml and in severe acute pancreatitis it was 3.62±1.9(mean±SD) µg/ml. The difference among the groups were statistically significant (table II; p<0.001). Thus serum D-dimer could predict disease severity early in the course of disease successfully.

Salomone et al.[12] reported that four times increase of D-dimer on admission could predict severe acute pancreatitis(SAP).

In the present study 55(63.2%) patients did not develop any kind of complications and serum D-dimer level at day 1 and day 3 were 2.4±1.73 and 0.81±0.49 respectively. On the other hand 32 (36.8%) patients developed complications and serum D-dimer level at day 1 and day 3 were 5.86±3.5 and 2.31±2.3 respectively. The difference among the groups were statistically significant (table III; p<0.001).That reveals serum D-dimer is a predictor of outcome of acute pancreatitis.

Radenkovic et al.[14] showed that D-dimer concentrations at admission and at 24 hours were predictive of in 91 patients with AP: 67 without OF and 24 with failure. Ke et al.[21] in their study found that patients who presented with MODS, pancreatic necrosis, secondary infection, or a positive blood culture showed higher maximum levels of D-dimer (p>0.001).Patients who died in hospital also had higher maximum levels of D-dimer.

This study showed that plasma levels of PT, APTT and fibrinogen were significantly higher in patients who had moderately severe to severe AP (table IV).

This findings support that coagulation abnormalities present in acute pancreatitis and is related to disease severity.

Radenkovic et al.[14] showed that patients who developed organ failure had significantly higher plasma levels of PT, APTT, INR, fibrinogen, PAI-1, and D-dimer and lower plasma levels of AT III, plasminogen, and protein C. Maeda et al.[10] in their study found that the markers of disseminated intravascular coagulation at admission were significantly associated with mortality (p < 0.0001).

ROC curve (figure 2) evaluating the role of serum D-dimer at day 1 in predicting severity of acute pancreatitis showed area under curve(AUC) was 0.867 which is statistically significant (p <0.001) (table V).Serum level of D-dimer at cut off point e"3.3µg/ml showed highest sensitivity (81.3%) & specificity (81.8%) (table VI). So serum D-dimer at day 1 could predict severity of acute pancreatitis successfully very early in the disease. On day 3 of admission ROC curve (figure 3) showed that the area under curve (AUC) was 0.838 and statistically significant (p <0.001) (table V) .The serum level of D-dimer at cut off point e"1.05 µg/ml on day 3 showed highest sensitivity (76.7%) & specificity (77.3%) (table VII).The sensitivity and specificity of serum D-dimer level for predicting the severity of acute pancreatitis was more on day 1 than day 3 (table VIII).

This findings is consistent with the findings of Radenkovic et al.[14] who showed that the sensitivity and specificity of D-dimers were 90% and 89% at admission and 90% and 81% at 24 hours, respectively for prediction of severity of acute pancreatitis.

The accuracy of D-dimer for prediction of severity of acute pancreatitis on day 1 with a cut off value ≥3.3 µg/ml and day 3 with a cut off value ≥1.05 µg/ml was 87.7 % and 82.7 % respectively (table VIII).

This study found that D-dimer at day 1 (cut off value e"3.3 µg/ml) and day 3 (cut off value ≥1.05 µg/ml) had a good sensitivity, specificity and accuracy for predicting outcome of acute pancreatitis.

Sensitivity, specificity and accuracy was 77.8%, 76.5% and 77.0% respectively at day 1 (cut off value ≥3.3 µg/ml) and it was 73.5%, 77.4% and 75.9% respectively at day 3 (cut off value ≥1.05 µg/ml) in prediction outcome of AP (table XI).

Maeda et al.[10] in their study reported sensitivity of 85% and specificity of 67% for D-dimer at hospital admission in predicting outcome of acute pancreatitis patients. In another study, Gomercic et al.[19] found that D-dimer levels predict AP complications with good sensitivity (81% at 48 hours and 74% at 36 hours).

This study found that D-dimer at day 1 and day 3, CRP, Glasgow score, BISAP score were significantly higher in the complicated group and moderately severe and severe acute pancreatitis. However, there was no difference in Ranson scores between them (table XII, table XIII). This is consistent with the findings of Gomercic et al[19] who showed that the median D-dimer (2866 vs 1616 ng/ml, p<0.001) and CRP levels (107.3 vs 75.6 mg/l, p<0.001) were significantly higher in the complicated group and no difference in Ranson scores between the two groups.

According to Spearman ranked correlations, serum D-dimer, Glasgow score and Ranson score of the patients with acute pancreatitis showed positive correlation with each pair of them (table XIV; p<0.001). Serum D-dimer also showed significantly positive correlation with BISAP score (p 0.017) and CRP levels (p 0.002) according to Spearman ranked correlation technique (table XIV). So D-dimer seemed to have predictive power similar to that of the present score system.

Limitations of the study

1. The study population was taken from one selected hospital in Dhaka city, so that the results of this study may not reflect the exact picture of the country.
2. Dependence on the patient, regarding the history.
3. Small sample size was also a limitation of the study.

Recommendations

Serum D-dimer measurement among patients with acute pancreatitis may be used as a predictor of severity and outcome of acute pancreatitis. Further studies with larger sample size are recommended.

Conclusion

This study evaluated the diagnostic efficacy of serum D-dimer in predicting severity and outcome of acute pancreatitis. The difference of serum D-dimer levels between mild, moderately severe and severe acute pancreatitis was statistically significant and it was also higher in patients who developed complications following acute pancreatitis than those without complications. This study showed that cut off value of serum D-dimer ≥3.3 µg/ml at day 1 and ≥1.05 µg/ml at day 3 may be used as a reliable laboratory parameter to predict severity in acute pancreatitis. In the present study serum D-dimer values at day 1 and day 3 are found to have a good sensitivity. The test can be used to determine the outcome of acute pancreatitis. This simple, feasible and reproducible marker can be used in clinical practice to improve the early management of acute pancreatitis.

Conflict of interest: Nothing to declare.

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