SCIENTIFIC ARTICLE

D-dimer: a predictor of acute pancreatitis

Gode D, Lamture Y.R
Datta Meghe medical college, Nagpur of DMIMS Deemed University, India

Keywords: Acute pancreatitis; D-Dimer; multiple organ dysfunction; pseudo cyst; sensitivity

Abstract

Introduction

Defect in coagulation present even in the early stage of acute pancreatitis. D-dimer is a small protein particle generated during blood clot disintegration due to lysis of fibrin. It is an accurate indicator of lysis of fibrin, so has an association with the severity of pancreatic inflammation. The study was undertaken to know the utility of d-dimer to forecast organ failure or complications in acute pancreatitis.

Methodology

From June 2019 to Jan 2020, 50 patients of acute pancreatitis were enrolled in this prospective study. Patients were subjected to the d-dimer test within 24 hours after admission. The patients were split into two groups; with organ failure (complications) and without any complications. The result of the d-dimer test was correlated with these groups.

Results

50 patients of acute pancreatitis were included in this study. Organ failure or local complications observed included impairment renal in 4 patients (16%), vasopressor requirement in 4(8%), pulmonary dysfunction in 5 (10%) and multiple organ failure syndrome (MODS) in 5 (10%). The sensitivity of d-dimer was 75% and specificity was 90%. Positive predictive value and negative predictive value of d-dimer were 91%, 74% respectively.

Conclusions

D-dimer is an accurate and cost-effective test to predict organ failure or local complications in a patient of acute pancreatitis.

Correspondence: Lamture Y.R
E-mail: yash18671@gmail.com
Received: 23-02-2020Accepted: 12-03-2020
http://orcid.org/0000-0002-4876-3686
DOI: http://doi.org/10.4038/sljs.v38i1.8670

Introduction

Acute pancreatitis is a disorder of inflammation of variable severity. It may fluctuate from mild disease to severe even associated with organ failure. Around one-fourth of the patients present as severe acute pancreatitis, with a mortality rate of up to 25%. Death in severe acute pancreatitis can occur in the early phase, secondary to an inflammation and later on, because of infection and major bleeding. Coagulopathy and obstructed microcirculation are common in the early disease and correlate with severity [1]. The diagnosis of acute pancreatitis is based on clinical features, serum amylase level and imaging like ultrasound and or contrast-enhanced computed tomography [2].

Patients with a mild form of pancreatitis need minimal medical attention, but those with moderate or severe forms need intensive care. So, it is vital to know the disease progression at an early phase of pancreatitis to halt it [3].

Acute pancreatitis is not an irreversible disorder. This inflammatory disorder leads to the release of tissue factors (prostaglandins), cytokines and activated complements. They stimulate coagulation and also stop lysis of fibrin, leading to a stage of hypercoagulation. Hence markers of disseminated intravascular coagulation, like d-dimer and antithrombin-III levels, may forecast disease progression. Fibrin disintegration products (d-dimer) have a pro-inflammatory action with leukocytes and can stimulate the vascular endothelial cells to secrete cytokines [4]. D-dimer is an investigation of choice to diagnose thromboembolism and has been found to have the ability to predict the outcome in acute pancreatitis [5]. It can be utilised to predict organ dysfunction or complications in severe acute pancreatitis patients [6].

Previous studies suggest coagulation related factors are potential predictors of severity and outcome of panceatitis [2,3,4]. Kumar MSA et al proved in his study that d-dimer can be used as a single predictor in pancreatitis [7].

Most of the cases of acute pancreatitis usually report to primary health centres, which lack facilities for resuscitation and supportive treatment for patients of severe acute pancreatitis. These patients can develop organ failure. So, their prompt referral to tertiary care centres would save time

Table 1. Demography with clinical details

Gender		Age groups affected in years		
Male	Female	20-40	40-60	60-80
45 (90%)	5 (10%)	38 (56%)	10 (20%)	2 (4%)
Aetiology			Progression of pancreatitis	
Alcohol	Idiopathic	Gall stone	Uncomplicated	Organ failure/ complications
44 (88%)	10 (20%)	1 (2%)	22 (44%)	Renal failure 4 (8%) Need of vasopressor 4 (8%) MODS 5 (10%) ARDS 5 (10%) Pseudocyst 10 (20%)

and reduce mortality and morbidity. Hence early recognition of organ failure at the primary level is beneficial for the patient. Most of the studies done are in favour of d-dimer being an effective predictor for organ failure in acute pancreatitis, but one study still has conflicting results regarding its efficacy [8], also the number of studies favouring d-dimer being an effective predictor of organ failure in severe acute pancreatitis are few [6].

Considering all these factors this study was undertaken to prove its efficacy to predict organ failure or complications in acute pancreatitis.

Aim:

To identify the efficacy of d-dimer to predict the severity of acute pancreatitis.

Materials and methods

It was a prospective study, including 50 participants of acute pancreatitis.

Study setting: Datta Meghe medical college, Nagpur (India) of Datta Meghe institute medical sciences deemed university

Study duration: June 2019- June 2020

Sample size: 50 patients

Inclusion criteria:

All patients of acute pancreatitis (age>18 years)

Exclusion criteria:

1. Recurrent attacks of acute pancreatitis.
2. History of surgery for pancreatitis.
3. Ischaemic heart disease, cerebrovascular accident, history of thromboembolism and history of the anticoagulant.

This study was conducted after approval of the Institutional Ethics Committee, Jawaharlal Nehru Medical College, Sawangi (Meghe).

Baseline data including name, age, sex and other investigations such as ultrasonography of abdomen, contrast-enhanced computed tomography (CECT) of the abdomen, serum amylase/lipase, serum calcium as per the requirement of the patient. D-dimer test was done within 24 hrs of admission.

Statistical analysis:

Statistical analysis of the d-dimer test was done by the software SPSS. Its correlation with organ failure and local complications was determined. Predicting power of d-dimer was determined by estimating true positive, false positive, true negatives and false negative. These were used to calculate the parameters of diagnostic accuracy sensitivity and specificity.

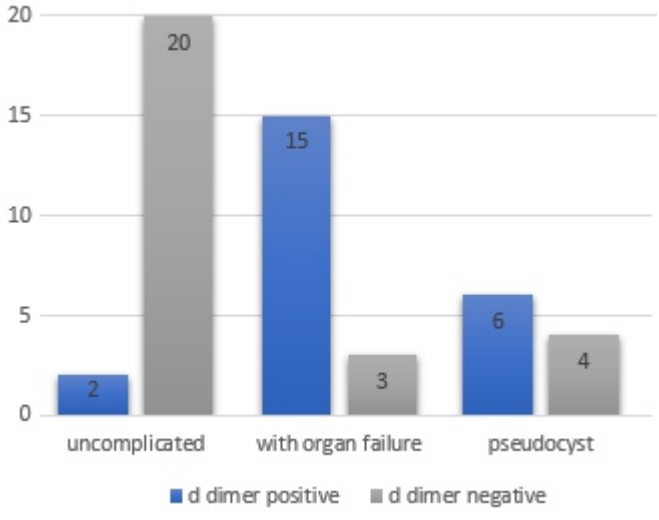

Figure 1. D-dimer test with complications or organ failure.

Results

Table 1 depicts demography with clinical details of patients. Around 50 acute pancreatitis patients participated in the study. Organ dysfunction during the episodes of pancreatitis was high: renal impairment in 4 patients (16%) a vasopressor requirement in 4(8%), pulmonary dysfunction (ARDS) developed in 5 (10%) and multiple organ failure syndrome (MODS) in 5 (10%) patient.

In most patients with organ failure or local complications, the d-dimer test was positive and in uncomplicated pancreatitis d-dimer test was negative (Figure 1). The sensitivity was 75%, and the specificity was 90%. The positive predictive value was 91% and the negative predictive value was 74%.

Discussion

The major difficulty in treating pancreatitis is to predict its severity. The present study has proved that the d-dimer test done on admission or within 24 hours after admission was valuable in the prediction of multiple organ dysfunction or complications (Table 1 and Figure 1).

Pathophysiology of acute pancreatitis has two components; systemic inflam-matory response syndrome and pancreatic necrosis which can be associated with infection and septic shock [9]. Severe acute pancreatitis outcome or prognosis solely depend on the presence of organ failure and infection of pancreatic necrosis. The present study proved the efficacy of the d-dimer test to forecast these two parameters of prognosis. Hence it can be used to select an individual patient for prompt aggressive treatment.

Radenkovic D. et al showed prothrombin time, fibrinogen, and d-dimer levels on admission were notably higher in organ failure and lower in non-organ failure patients. A d-dimer value of 414.00 microgram/L was the best cut off level to forecast organ failure. Sensitivity was 90% and specificity was 89%. The positive predictive value of d-dimer was75% with negative predictive value was 96% [2], suggestive of the d-dimer test's accuracy to identify prognosis of pancreatitis. This study was similar to the present study.

A study done by Salomone T et al showed mildly elevated d-dimer levels in (1.5 times of normal) in patients of pancreatitis without complications. But with organ failure, these levels increased to seven times above the normal. They suggest that d-dimer had definite a role to forecast the prognosis of pancreatitis and the possibility of systemic involvement [5].

Lu Ke et al showed higher levels of d-dimer in patients with multiple-organ failure, need for surgical treatment, and in the presence of pancreatic necrosis. Levels of d dimer were lower in a patient of mild disease. This suggests a positive prediction of d dimer about organ failure or local complications of pancreatitis [6]. Results of this study were similar to the present study,

Maeda K et al [8] showed less favourable results of a d-dimer test than the antithrombin III level [8] in a prediction of prognosis of pancreatitis. This study was not similar to the present study.

Etiopathology of raised levels of d-dimer is difficult to understand. The severity of pancreatitis is depending on the extent of obstruction of pancreatic microcirculation due to microthrombi formation with fibrinolysis. Severe coagulative disorder suggested by a positive d dimer test, usually associated with increase possibility of pancreatic necrosis and organ failure [6]. This could be positively correlated with a d-dimer test.

Conclusion

D-dimer is an accurate and cost-effective test to predict organ failure or local complications due to acute pancreatitis.

Limitation

We didnt have the facility to measure d-dimer levels, hence it was not possible to find out cut off level of d-dimer to forecast prognosis of acute pancreatitis.

All authors disclose no conflict of interest. The study was conducted in accordance with the ethical standards of the relevant institutional or national ethics committee and the Helsinki Declaration of 1975, as revised in 2000.

References

1. Ning Yang, Dong-Lei Zhang and Jian-Yu Hao, Coagulopathy and prognostic potential of d-dimer in hyperlipidaemia-induced acute pancreatitis. Hepatobiliary pancreatic disease international, December 15, 2015, vol 14(6).:633-641. https://doi.org/10.1016/s1499-3872(15)60376-9
2. Radenkovic D, Bajec D, Ivancevic N, Milic N, Bumbasirevic V, Jeremic V, et al. D-dimer in acute pancreatitis: a new approach for an early assessment of organ failure. Pancreas 2009 Aug;3(6):655-60. https://doi:10.1097/MPA.0b013e3181a66860
3. Hanna Sternby, Hannes Hartman, Dorthe Johansen, Henrik Thorlacius, Sara Regnér, Chronological pathophysiological patterns of biomarkers in acute pancreatitis, Pancreatology Jun 2016, 16(3), S52. https://doi.org/10.1016/j.pan.2016.05.179
4. Paulina Dumnicka, DawidMaduzia, PiotrCeranowicz, Rafał Olszanecki, Ryszard Drożdżand Beata Kuśnierz-Cabala. The interplay between inflammation, coagulation and endothelial injury in the early phase of acute pancreatitis: clinical implications.Int. J. Mol. Sci. 2017, 18,354 https://doi.org/10.3390/ijms18020354
5. Salomone T, Tosi P, Palareti G, Tomassetti P, Migliori M,

Guariento A, et al. Coagulative disorders in human acute pancreatitis: role for the D-dimer. Pancreas 2003, 26(2), 111–116 https://doi.org/10.1097/00006676-200303000-00003

6. Lu Ke, Hai-bin Ni, Zhi-hui Tong, Wei-qinLi, Ning Li, Jie-shouLi.D- dimer as a marker of severity in patients with severe acute pancreatitis. Japanese society of hepato-biliary-pancreatic surgery & springer 2011, J HepatobiliaryPancreatSci 2012, 19:259–265. https://doi.org/10.1007/s00534-011-0414-5
7. Anil Kumar, Ranjith Kothagattu, D-dimer levels in predicting the severity of acute pancreatitis. IntSurg J 2017; 4:3993-8. https://doi.org/10.18203/2349-2902.isj20175398
8. Maeda K, Hirota M, Ichihara A, Ohmuraya M, Hashimoto D, Sugita H, et al. Applicability of disseminated intravascular coagulation parameters in the assessment of the severity of acute pancreatitis. Pancreas. 2006;32(1):87-92. https://doi.org/10.1097/01.mpa.0000186248.89081.44
9. Jones AE, Trzeciak S, Kline JA. The sequential organ failure assessment score for predicting outcome in patients with severe sepsis and evidence of hypoperfusion at the time of emergency department presentation. Crit Care Med. 2009;37(5):1649-54. https://doi.org/10.1097/ccm.0b013e31819def97