
Comparison of D- Dimer & FDP (Fibrin Degradation Product) with APACHE II as marker of Severity of Acute Pancreatitis

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Abstract

Acute Pancreatitis is an acute inflammatory process of the pancreas with varying involvement of regional tissues or remote organ systems. Complex clinical criteria of Severe Acute Pancreatitis include Ranson's criteria for non-gall stone pancreatitis. The Apache II & multiple organ system failure scale provides prognosis at the time of admission. D Dimer Is a fragment produced during the degradation of clot. FDP is Fibrin Degradation Product in blood which results from dissolution of clot. The Study was conducted at Chugh Multispecialty Hospital, Bhiwani in 103 patients fulfilling the inclusion and exclusion criteria for a period of 1 Year. The Result Concludes APACHE II FDP & D - Dimer values significantly correlate with each other in almost all aspects.

Keywords: APACHE-II; D-Dimer; FDP; Pancreatitis; MODS.

Introduction

Acute pancreatitis is an acute inflammatory process of the pancreas with varying involvement of regional tissues or remote organ systems. The incidence of acute pancreatitis in England, Denmark and USA ranges between 5 & 30 per 100,000 population with highest incidence recorded in the United States and Finland.

The estimated incidences are however inaccurate because the diagnosis of mild diseases may be missed and death may occur before diagnosis in 10% of people with severe disease [1].

The increased incidence of pancreatitis, coupled with new treatment options, poses a challenge for primary care physicians. Twenty five percent of patient suffer from the severe form of the disease with local or systemic complications, resulting in mortality rate ranging from 2 -10%.

Increased mortality and morbidity are associated with organ failure in 50% of severe acute pancreatitis cases [2].

The two most common causes of acute pancreatitis are cholelithiasis and alcohol. The other causes includes drugs (Azathioprine, Corticosteroids, etc.) [3].

Regardless of the etiology, pancreatic enzymes (Including Trypsin, Phospholipase A₂ & Elastase) become activated within the gland itself. The enzymes can damage tissue and activated complement and inflammatory cascade, producing cytokines. This process causes inflammation, edema, and sometimes necrosis. In mild pancreatitis, inflammation is confined to the pancreas; the mortality rate is 10 to 50%. After 5 to 7 days, necrotic pancreatic tissue may become infected by enteric bacteria. The chances of developing infected pancreatic necrosis depend the extent of necrosis [4].

Activated enzymes and cytokines that enter the peritoneal cavity cause a chemical burn and results in exudation of fluid in third space; those that enter the systemic circulation causes a systemic inflammatory response that can result in acute respiratory distress syndrome and renal failure. The systemic effects are mainly the result of

increased capillary permeability and decreased vascular tone, which result from the released cytokines and chemokines. Phospholipase A₂ is thought to injure alveolar membranes of the lungs [4].

In about 40% of patients, collections of enzymes rich pancreatic fluid and tissue debris form in and around the pancreas and are called acute fluid collection. In about half, the collection resolves spontaneously. In others, the collections become infected or form pseudocysts. Pseudocysts may bleed rupture or become infected [5].

Death during the first several days is usually caused by cardiovascular instability (With refractory Shock & Renal Failure) or respiratory failure (With Hypoxemia and at times adult respiratory distress Syndrome).

Occasionally, death results from heart failure secondary to an unidentified myocardial depressant factor.

Death after the first week is usually caused by Multi organ system failure and / or infected necrosis and septic complication [6].

Pancreatitis is classified as acute unless there are CT/MRCP or ERCP findings of chronic pancreatitis. Mild acute pancreatitis consists of minimal or no organ dysfunction and an uneventful recovery. Severe pancreatitis manifests as organ failure and local complications such as necrosis, abscess and pseudocyst [7].

Complex clinical criteria of severe acute pancreatitis include Ranson's criteria for non gall stone pancreatitis and APACHE 2 (Acute Physiology and Chronic Health evaluation) score more than [8]. The APACHE 2 and the multiple organ system failure scales provides prognostic information at the time of admission and may be repeated daily to monitor disease progression.

It has been shown that coagulation abnormalities are common in acute pancreatitis which might be a part of the inflammatory process or related to early intravascular consumption of coagulation factors secondary to circulating pancreatic enzymes, particularly Trypsin or secondary to any vascular injury [9].

D - Dimer is a fragment produced during the degradation of Clot. The D Stands for Domain indicates two identical units or domains. D- Dimer level is related to disease severity. FDP is a test measures Fibrin Degradation products in blood which result from dissolution of clots.

As a result of the coagulation process, fibrinogen is split in to Fibrin monomer and Fibrin. Fibrin

monomer forms the fibrin polymer clot. By Measuring FDPs and idea about the activity of fibrinolytic system can be achieved [10].

A positive D - Dimer indicates the presence of an abnormally high level of fibrin degradation products in the body. There is sparse literature of D - Dimer and FDP as markers of severe pancreatitis [11].

Aims & Objectives

1. To study the profile of D - Dimer & FDP in acute pancreatitis.
2. To compare serum D Dimer and FDP levels with the APACHE II.

Review of Literature

Acute Pancreatitis is associated with increased concentration of serum fibrinogen, FDPs & D - Dimer, representing acquired dysfibrinogenemia, which is impaired fibrin polymerization. These coagulation abnormalities in patients with AP may be related to early intravascular consumption of coagulation factors secondary to circulating pancreatic enzymes like trypsin or secondary to vascular injury [10].

D Dimer may be expression of pancreatitis involving other organ systems. D- Dimer was found to be a prominent link in the chain of events leading to severe disease and statistically significant difference was found in the level of D - Dimer between uncomplicated and complicated pancreatitis [12].

Berry et al reported elevated levels of FDPs in 45% of patients with acute pancreatitis and suggested that the marked lung damage may be related to pulmonary fibrin deposition. Studies have shown reduced level of protein C, Anti thrombin III, D- Dimer and PAI - 1 in severe necrotizing pancreatitis indicating exhaustion of fibrinolysis and coagulation inhibitors in patients with poor outcome [13].

Material & Methods

This study was conducted at Chugh Multispecialty, Bhiwani for a period of one year.

Inclusion Criteria

All patients with a diagnosis of acute pancreatitis with or without complications were included.

Exclusion Criteria

1. Patient who presented after one week of onset of pain.
2. Underlying significant co morbidities including.
 - Decompensated Liver Disease.
 - Pre Existing Pulmonary infection or active pulmonary pathology.
 - Patients with inherent bleeding disorders or coagulation abnormalities.
 - Pregnant females.
 - Patients with active cardiac diseases e.g acute myocardial infarction, USA & Atrial fibrillation.
 - CKD - Chronic Kidney Disease.

Diagnostic Criteria

Acute Pancreatitis was diagnosed based on presence of characteristic pain and more than 3 times elevation of amylase /Lipase. Patients underwent a thorough history taking and clinical examination.

The following investigation were performed

- Complete Hemogram.
- Serum Amylase & Serum Lipase level.
- Liver Function Test.
- Renal Function Test.
- PT - Prothrombin Time.
- Urine Routine & microscopy.
- ABG - Arterial Blood Gases.
- USG - Abdomen.
- CECT - Abdomen if required.

D- Dimer And FDP Levels were done on 1, 3 & 7th Day of admission and then 7th day till the time of discharge or death.

Similarly APACHE Scores were calculated on the aforementioned days using the computer based APACHE II calculator. CECT was done on 3rd and 5th day in patients where indicated. Day of onset of organ failure from the onset of pain and number of organ involved were recorded.

Severity of pancreatitis was taken as per APACHE II scores of <8 as mild and >8 as severe. FDP <10 and D - Dimer <200 were taken normal.

Statistical Analysis

A database was generated in SPSS software. Correlation between D Dimer And FDP with APACHE II scores were expressed as person's correlation coefficient.

Comparison between the variables was done using mann- Whitney test, Chi square Test. A P- Value <0.05 was considered as statistically significant.

Results & Observations

One Hundred three (103) patients presenting with acute pancreatitis who fulfilled the inclusion criteria were included in the study.

Their details are as follows.

- Alcohol was the commonest etiology of the acute pancreatitis.
- In almost 25% of patients the etiology was not clear during their admission.
- Out of 103 patients taken together, 97 survived and 6 died with an approximate survival rate of 97.17%. Among the organ failure, respiratory failure was most common i.e. in 25 patients (25%), renal failure in 8 patients (8.08%), hypotension was present in 5 patients (5.2%). One patient had episode of gastro intestinal bleed.

Table 1: Organ Failure & Mortality

Organ Failure & Mortality	
Variables	All patients
Respiratory Failure	25 (25.0%)
Renal failure	8 (8.08%)
Bleed	1 (1.04 %)
Hypotension	5 (5.21 %)
Death	6 (5.38 %)

In this study we have tried to find any correlation with outcome of the patient i.e. whether the patient survives or dies with the severity of scores of APACHE and with the values of FDP and D- Dimer. Results shown above clearly depict that in the patient who died had higher APACHE scores, higher FDP values and higher D- Dimer values in all the 3 readings taken, which shows that they are correlated significantly with p value < 0.05 on all the occasions.

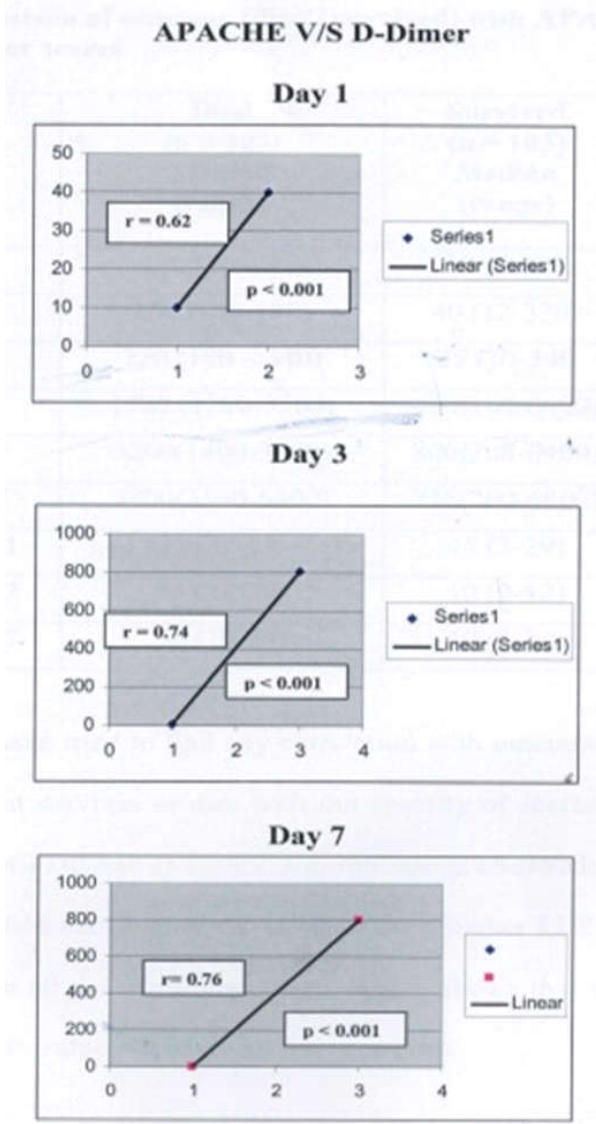


Fig. 1: APACHE V/S D- Dimer

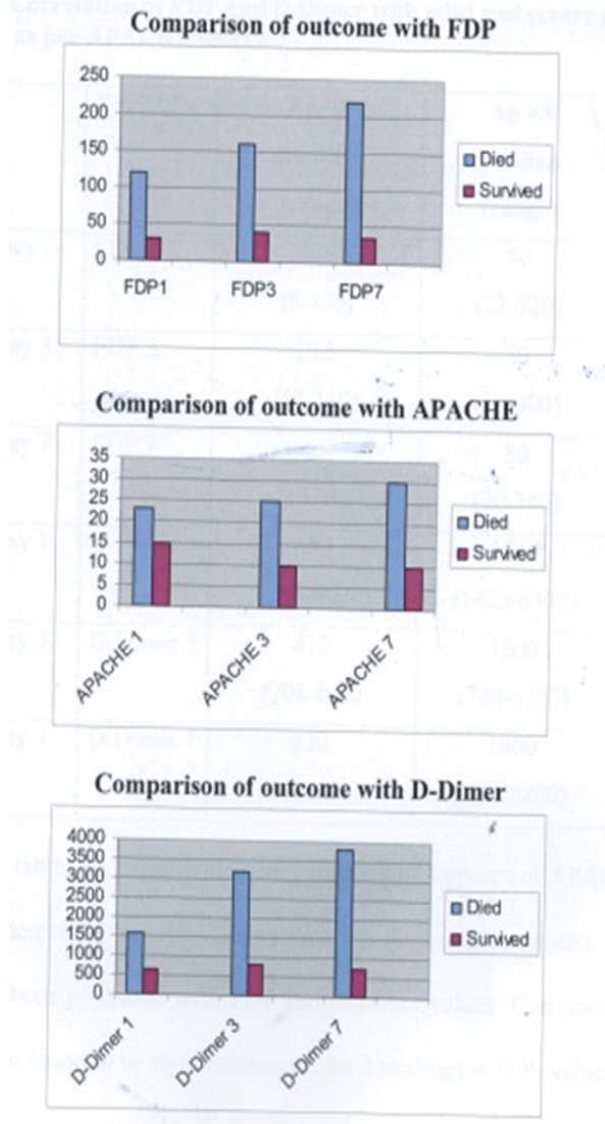


Fig. 2: Correlation of outcome with FDP, APACHE and D-Dimer

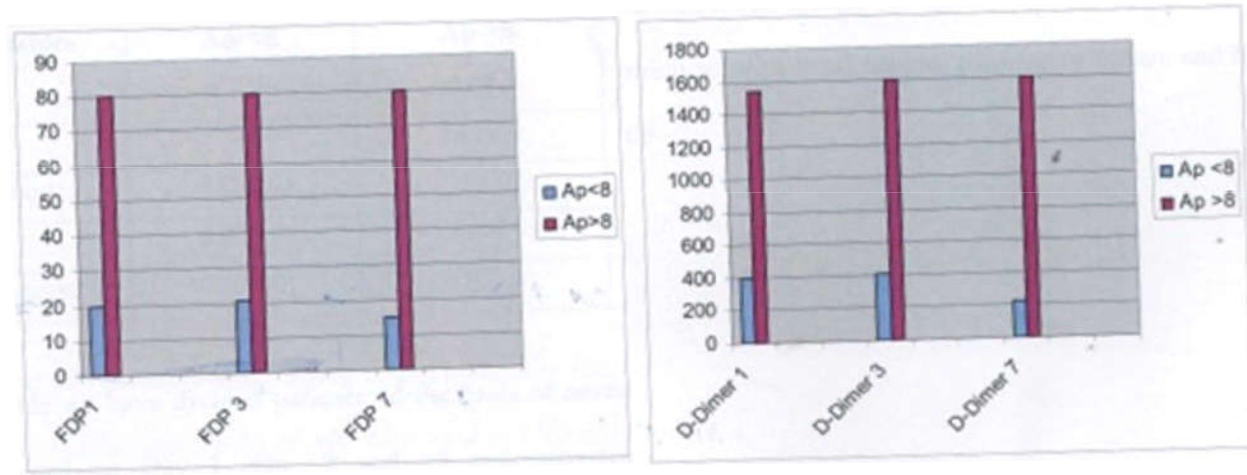


Fig. 3: Correlation of FDP and D-Dimer with mild and severe pancreatitis as per APACHE scores

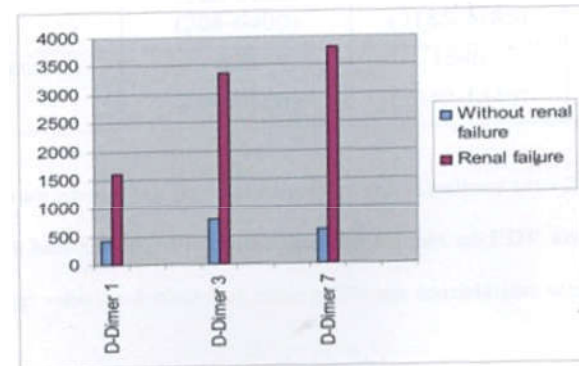
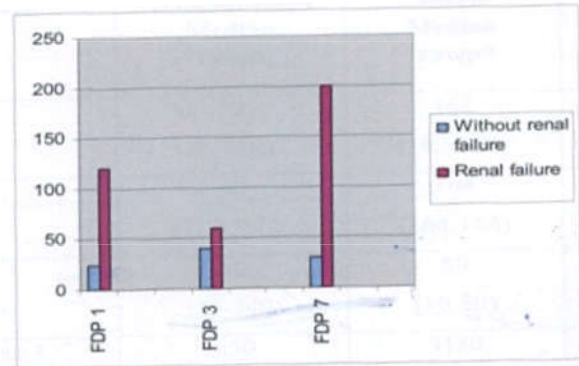
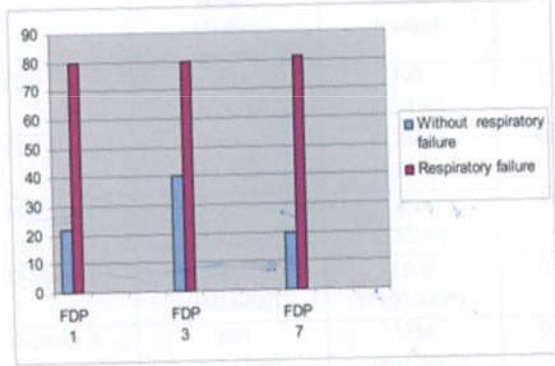


Fig. 4: Comparison of FDP and D-Dimer with respiratory failure

Fig. 5: Comparison of FDP and D-Dimer with renal failure

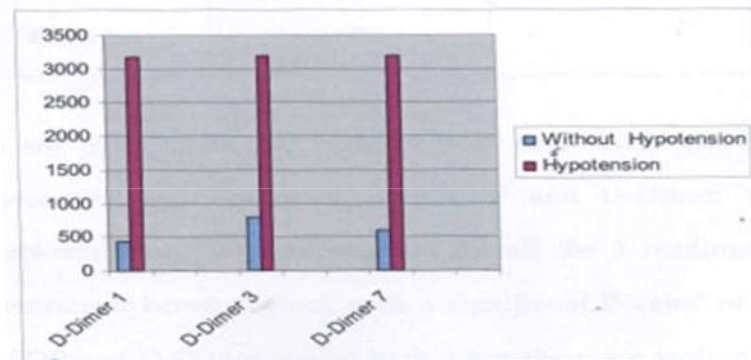
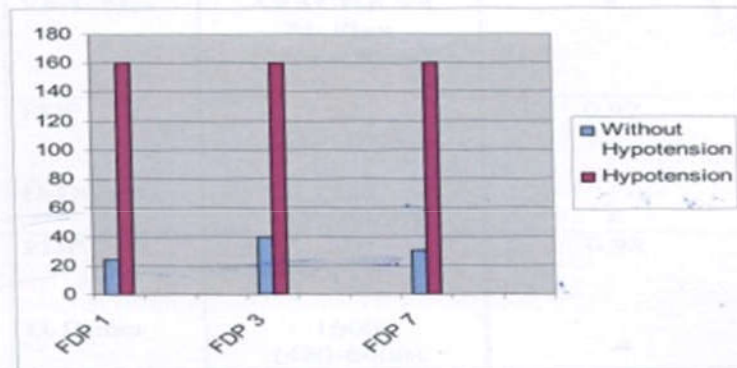


Fig. 6: Comparison of FDP and D-Dimer with Hypotension

Discussion

Acute Pancreatitis is associated with a wide range of clinical presentation varying from mild to severe clinical course with an overall mortality of about 10-15%. There is a need for an easier and more useful marker of severity, which is reliable and as good as APACHE II scoring in predicting severity, prompted us to conduct this study in our institute.

In our study the average age of presentation of patient with acute pancreatitis was 43 years.

In our group of patients maximum organ failure was seen around 3rd day of onset of pain. In our study we found most common etiological factor was alcohol which may be due to high frequency of male patients (70-87%).

We have found in our study that direct correlation exist between APACHE II scores with D- Dimer & FDP value taken on any day. We also found significant correlation between APACHE II scores FDP & D - Dimer values when patients were divided into Mild & Severe Pancreatitis. FDP & D - Dimer values were significantly correlated with incidence of organ failure specifically respiratory, Renal & cardiovascular failure in form of hypotension.

Higher FDP & D- Dimer values directly correlates with severity of pancreatitis because when we compared FDP and D -Dimer with Severe pancreatitis as per APACHE II scores.

We have also found that there is no correlation between FDP & D - Dimer with day of organ failure, CT Severity Index or total duration of stay in hospital for a patient.

Conclusion

Incidence of acute pancreatitis is more common in males, with alcohol consumption is the main etiological factor. In females biliary pancreatitis is more common. Organ failure are more common in first week after the attack of acute pancreatitis.

Among the organ failures, respiratory problems take the front seat, then comes the renal failure & hypotension.

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