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Original Research Article

# Study of D-DIMER in Severe Acute Pancreatitis in Andhra Pradesh Population

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**Abstract:**

**Background:** Coagulative disorder is known to occur in the early phase of severe acute pancreatitis (SAD), and D-dimmer is a commonly used clinical parameter of hemostasis. The plasma D-dimmer level is a biomarker of severity of acute pancreatitis.

**Method:** 75 patients with AP (Acute Pancreatitis) were admitted with an APACHE-II score. MODS pancreatitis necrosis was diagnosed by a CE CT APACHE-II score assessed daily during 1. 35 days after admission. Apart from S. D-dimmer, S. creatinine, S. bilurubin, S. urea nitrogen, and CRP levels were also studied. The stay at the hospital and ICU were also recorded.

**Results:** The aetiology was 45 (60%) biliary origin, 14 (18.6%) alcohol abuse, 8 (10.6%) hyperlipidemia, and 8 (10.8%) idiopathic. The APACHE-II score was 9 (8–11), and the Ranson score 48 hours after admission was 4 (3-6). CRP level, 150 (103-201) Balthazar Index 6 (5-70), 9 (12%) hospital mortality, 60 (80%) pancreatic necrosis, 23 (30.6%) pancreatic infection, 51 (68%) organ dysfunction, 27 (36%) MODS, 14 (18.6%) surgical intervention, 15 (9.5 to 25) duration of hospital stay, 10 (4 to 18) ICU stay (days) comparison of mean values of D0dimmer in relation to the presence of variable were highly significant ($p<0.001$).

**Conclusion:** A serum D-dimmer level study in severe acute pancreatitis helps to predict the severity of pancreatitis. It is an easy and inexpensive biomarker.

**Keyword:** Multiple Organ Dysfunction Syndrome (MODS), APACHE-II score, Ranson score, Andhra Pradesh.



## Introduction

Acute pancreatitis (AP) is a common clinical acute abdominal disease that has a narrow therapeutic window. Currently, AP is classified as mild acute pancreatitis (MAP), moderately severe AP (MSAP), and severe AP [1]. The majority of patients have mild symptoms of the disease and recover well, but approximately 20% develop SAP, which has a high mortality rate of 15–35, mainly due to pancreatitis necrosis, systemic inflammation, and persistent multiple organ dysfunction associated with concurrent infections [2]. In addition, the annual incidence of AP has increased along with medical costs, and AP is one of the leading causes of hospital deaths in developing countries [3]. Early treatment, for which early diagnosis and assessment of AP severity are essential, has been shown to reduce mortality rates. Currently, however, no method of effectively detecting disease severity is available. Various laboratory markers have been used to predict AP severity; performing CT upon admission solely to assess AP severity is not recommended, and radiological tests are expensive to perform. The D-dimmer levels are an indicator of AP severity [4]. Hence, an attempt was made to study the levels of D-dimmer along with various laboratory parameters and score values.

## Material and Method

75 patients admitted to the gastroenterology department of Andhra Medical College Hospital, Vishakhapatnam, Andhra Pradesh, were studied.

**Inclusive Criteria:** The patients are over the age of 18. Patients within 75 hours of the onset of clinically diagnosed severe pancreatitis were included in the study.

**Exclusion Criteria:** Patients who had suffered prior attacks, undergone surgical intervention, had a history of co-agulative disorders, or had a recent history of myocardial infarction or cerebral infarction were excluded from the study.

**Method:** Detailed history of age, sex, and aetiology The Ransome score and the APACHE-II score were recorded during admission. The definition of organ dysfunction was based on a score of multiple organ dysfunction syndromes (MODS). Pancreatitis necrosis was diagnosed according to the result of contrast-enhanced computed tomography (CECT). The APACH-II score was assessed on a daily basis during 1, 3, and 5 days after admission. The development of local complications, such as vasoactive drugs and mechanical ventilation, the duration of hospital and ICU stays, and the need for surgical intervention were also recorded.

In every patient, the plasma D-dimmer level was determined on admission and the 3rd, 5th days. The upper limit of the reference interval for D-dimmer was 500 microg/L. The maximum level of D-dimmer was defined as the highest level reached in all measurements, and the mean D-dimmer was defined as the mean level of all measurements. In addition, routine laboratory parameters such as serum concentrations of S. creatinine, S. bilirubin, urea nitrogen, and C-reactive protein (CRP) were also determined, along with D-dimmer levels. All patients received standard medical therapy and were followed until discharge from the hospital or hospital death.

The duration of the study was May 2020 to June 2021.

**Statistical analysis:** Demographic data and clinical manifestations were classified by percentage. Maximum values of D-dimmer were compared in the presence or absence of clinical variables, and a t test was applied for statistical analysis. The statistical analysis was carried out in SPSS 2007 software. The ratio of males and females was 2:1.

**Observation and Results**

**Table 1:** Demographic manifestation clinical manifestation – 45 (60%) were biliary origin, 14 (18.6%) alcoholic abuse, 8 (10.6%) hyper lipidemia, 8 (10.6%) Idiopathic.

APACH-II score – 9 (8-11), Ranson score – 48 hours after Admission – 4 (3-6), 150 (103-201), CRP (mg/d) on admission, Balthazar Index – 6 (5-7), Hospitality mortality 9 (12%), 60 (80%) Pancreatic necrosis, 23 (30.6%) pancreatic infection, 51 (68%) organ dysfunction, 27 (36%) MODS, 14 (18.6%) surgical intervention, 15 (9.5 to 25) (days) duration of hospital stay,10 (4 to 18) (days) duration of ICU.

**Table 2:** Value of maximum D-dimmer in relation to presence or absence of clinical variable –

- 9 deaths in the presence of 2158 (1552 – 2450)
- 13 patients required operative intervention – 2198 (1958-2518)
- 27 MODS – 1863 (1013-2218)
- 15 Needs for Vaso active drugs 2028 (1568-2453)
- 23 had secondary infection 1898 (1312-2240)
- 60 had pancreatic necrosis 1013 (785-1818)
- 17 need for mechanical of ventilation 2093 (1625-2353)
- 12 had positive blood cultures 2238 (1938-2668)

**Table 3:** Comparison of mean values of D-dimmer in relation of the presence or absence of clinical variables –

- Death 9 (1468-1989) 1821 (± 86.8) absence, 66 (426-902) 63.3 (± 79.3), t test was 41.1 and pM0.001
- Operation intervention required 13 (1609-2142) 18.50 (± 88.8) absence, 62 (418-780) 61.8 (± 60.3), t test was 60.2 and p<0.02
- 27 MODS (850-1866) 14.90 (± 169.3), test was 35.5 and p<0.001
- 15 need for vaso-active drugs (1392-1980) 16.50 (± 98.0) absence of vaso-active drugs (414-760) 616 (± 57.7) t test was 52.19, and p<0.001.
- 23 had secondary infection (1185-1934) 1520 (± 124.8) in the presence of D-dimmer, (405-698) 53.5 (± 48.7), t test was 48.4 and 9<0.001
- 50 had pancreatic necrosis (615-1470) 760 (± 132.4) in the presence of D-dimmer t test was 9.96 and p<0.01
- 17 Need for mechanical ventilation (1419-2110) 1736 (± 115.1), 58 (451-755), 615 (± 50.7) don't need for mechanical ventilation, t test was 56.7 and p<0.01.
- 12 had positive blood culture (1651-2158), 1881 (± 84.3) 63 (421-802) 623 (± 63.4) had negative blood culture, t test was 58.61 and p<0.01.

**Study of D-Dimmer in severe acute pancreatitis**

**Table 1: Demo-graphic data and clinical Manifestations (No. of Patients: 75)**

| Clinical manifestation | Aetiology | No | Percentage (%) |
|---|---|---|---|
| Aetiology | Biliary origin | 45 | 60 |
| | Alcohol abuse | 14 | 18.6 |
| | Hyperlipidmia | 8 | 10.6 |
| | Idiopathic | 8 | 10.6 |
| APACHE II score | 9 (8 – 11) | | |
| Ranson score 48 hrs after admission | 4 (3 – 6) | | |
| CRP level on admission (mg/α) | 150 (103 – 201) | | |

| | |
|---|---|
| Balthazar Index | 6 (5 – 7) |
| Hospital Mortality | 9 (12%) |
| Pancreatic Neurosis | 60 (80%) |
| Pancreatic infection | 23 (30.6%) |
| Organ dysfunction | 51 (68%) |
| MODS | 27 (36%) |
| Surgical intervention | 14 (18.6%) |
| Duration of Hospital study (days) | 15 (9.5 to 25) |
| Duration of ICU (days) | 10 (4 to 18) |

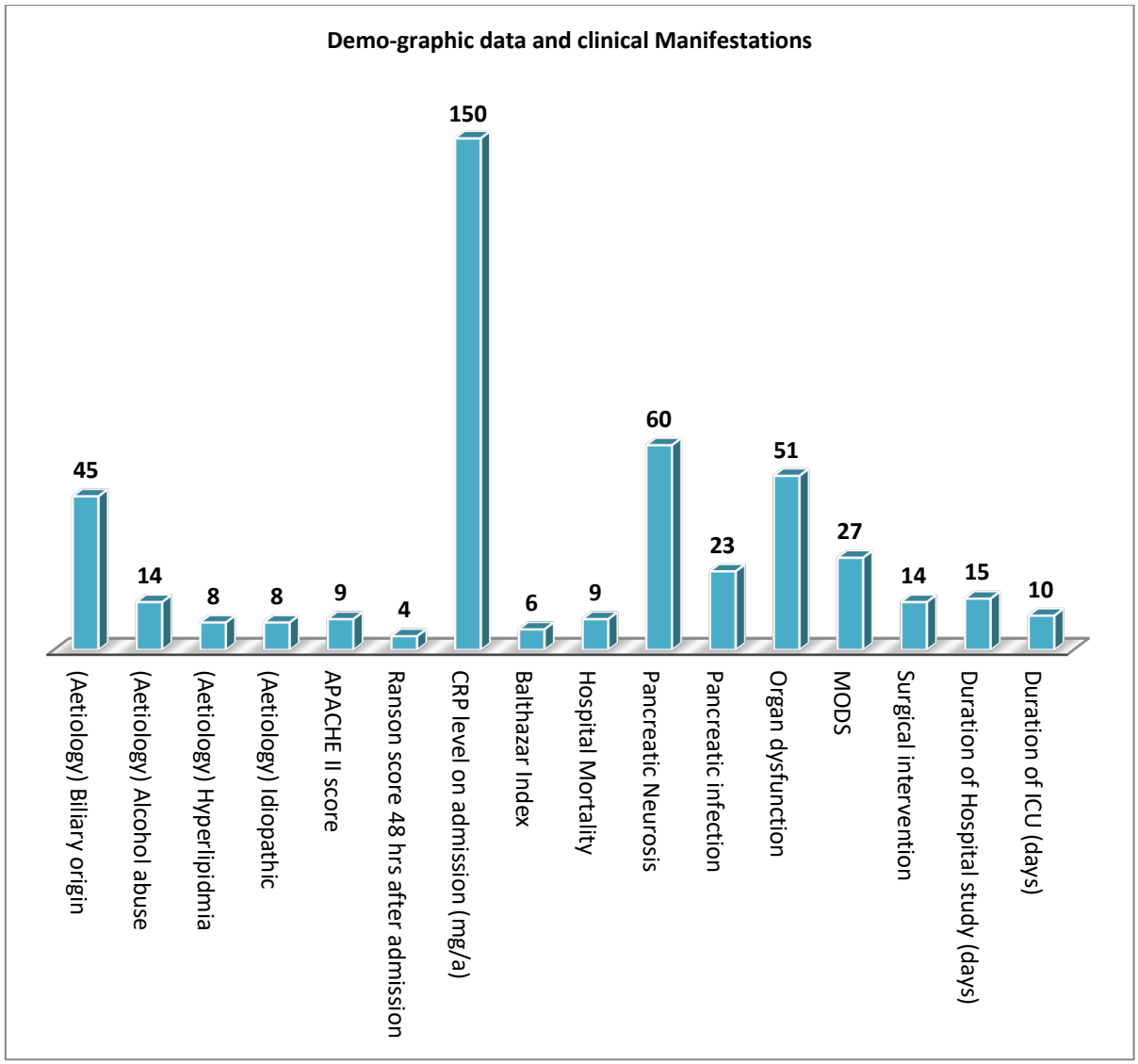


**Figure 1: Demo-graphic data and clinical Manifestations**

**Table 2: Values of maximum D-Dimer in relation to Presence or Absence of clinical variables (No. of Patients: 75)**

| Clinical variable | Presence | No | Absence | No |
|---|---|---|---|---|
| Death | 2158 (1552-2453) | 9 | 1832 (1168-5505) | 66 |
| Operative intervention required | 2198 (1758-2563) | 13 | 808 (528-1038) | 62 |
| MODS | 1863 (1013-2218) | 27 | 728 (448-938) | 48 |
| Need for Vaso active drugs | 2028 (1568-2453) | 15 | 793 (518-1015) | 60 |
| Secondary infection | 1898 (1312-2240) | 23 | 728 (458-938) | 52 |
| Pancreatic Necrosis | 1013 (785-1818) | 60 | 448 (318-618) | 15 |
| Need for Mechanical ventilation | 2093 (1625-2353) | 17 | 779 (508-1018) | 58 |
| Positive blood cultures | 2238 (1938-2668) | 12 | 813 (538-1023) | 63 |

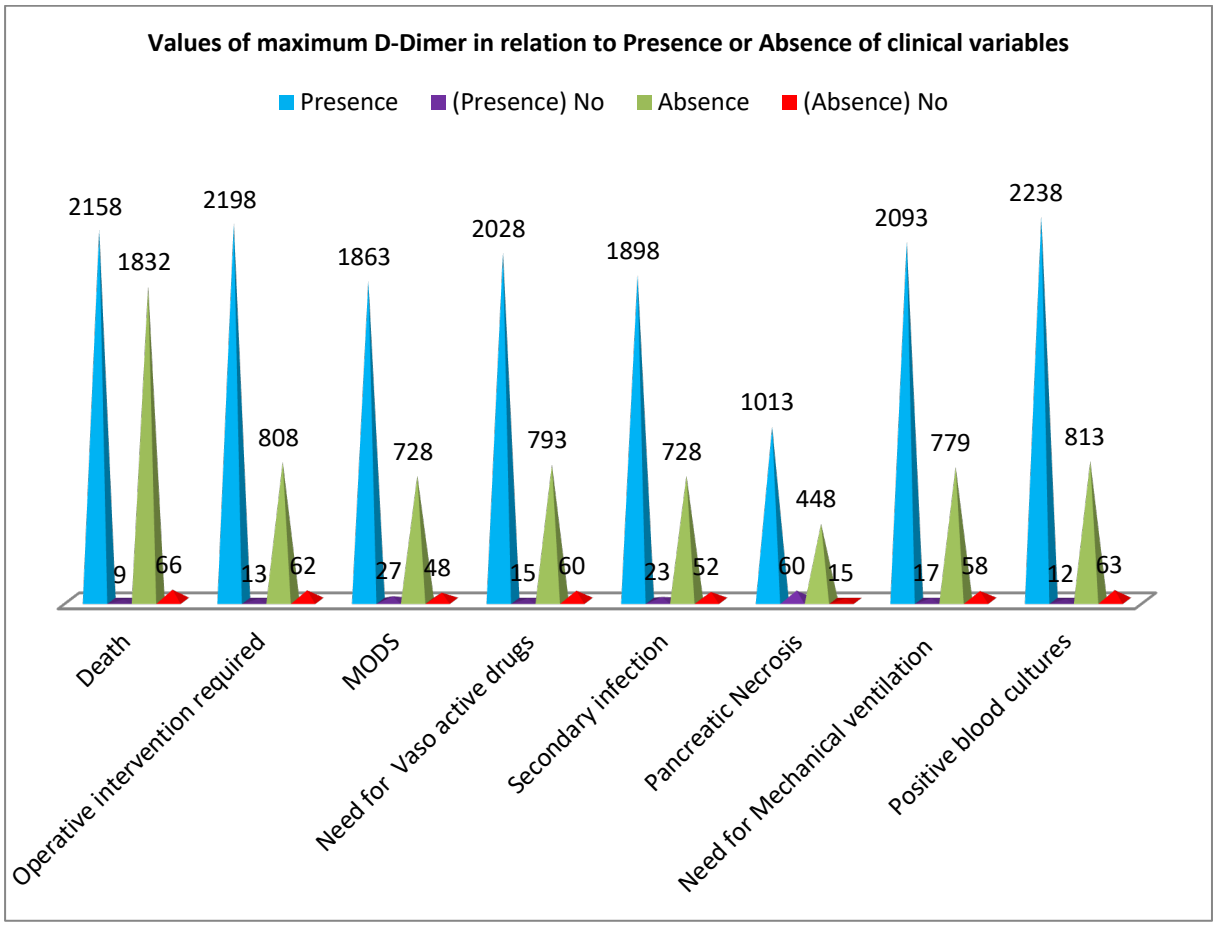


**Figure 2: Values of maximum D-Dimer in relation to Presence or Absence of clinical variables**

**Table 3: Comparison of Mean values of D-Dimmer in relation to the presence or absence of clinical variables (No. of Patients: 75)**

| Clinical variables | Presence D-Dimer µg/l (Mean ± SD) | Number | Absence D-Dimmer µg/l (Mean ± SD) | Number | p values |
|---|---|---|---|---|---|
| Death | 1821 (±86.8) (1468-1989) | 09 | 633 (±79.3) (426-902) | 66 | t=41.1 P<0.01 |
| Operation intervention required | 1850 (±88.8) (1609-2142) | 13 | 618 (±60.3) (418-780) | 62 | t=60.25 P<0.01 |
| MODS | 1490 (±169.3) (850-1866) | 27 | 535 (±53.3) (395-715) | 48 | t=35.55 P<0.01 |
| Need for vaso active drugs | 1650 (±98.0) (1392-1980) | 15 | 616 (±57.7) (414-760) | 60 | t=52.19 P<0.01 |
| Secondary infection | 1520 (±124.8) (1185-1934) | 23 | 535 (±48.7) (405-698) | 52 | t=48.42 P<0.01 |
| Pancreatic necrosis | 760 (±132.4) (615-1410) | 60 | 411 (±39.2) (259-494) | 15 | t=9.96 P<0.01 |
| Need for mechanical ventilation | 1736 (±115.1) (1419-2110) | 17 | 615 (±50.7) (451-755) | 58 | t=56.76 P<0.01 |
| Positive blood culture | 1881 (±84.5) (1651-2158) | 12 | 623 (±63.4) (421-802) | 63 | t=58.61 P<0.01 |

*t: Unpaired T test, P<0.01: Highly significant difference. Statistically there is significantly low value of D-Dimmer observed in clinically absent variables (P<0.01).

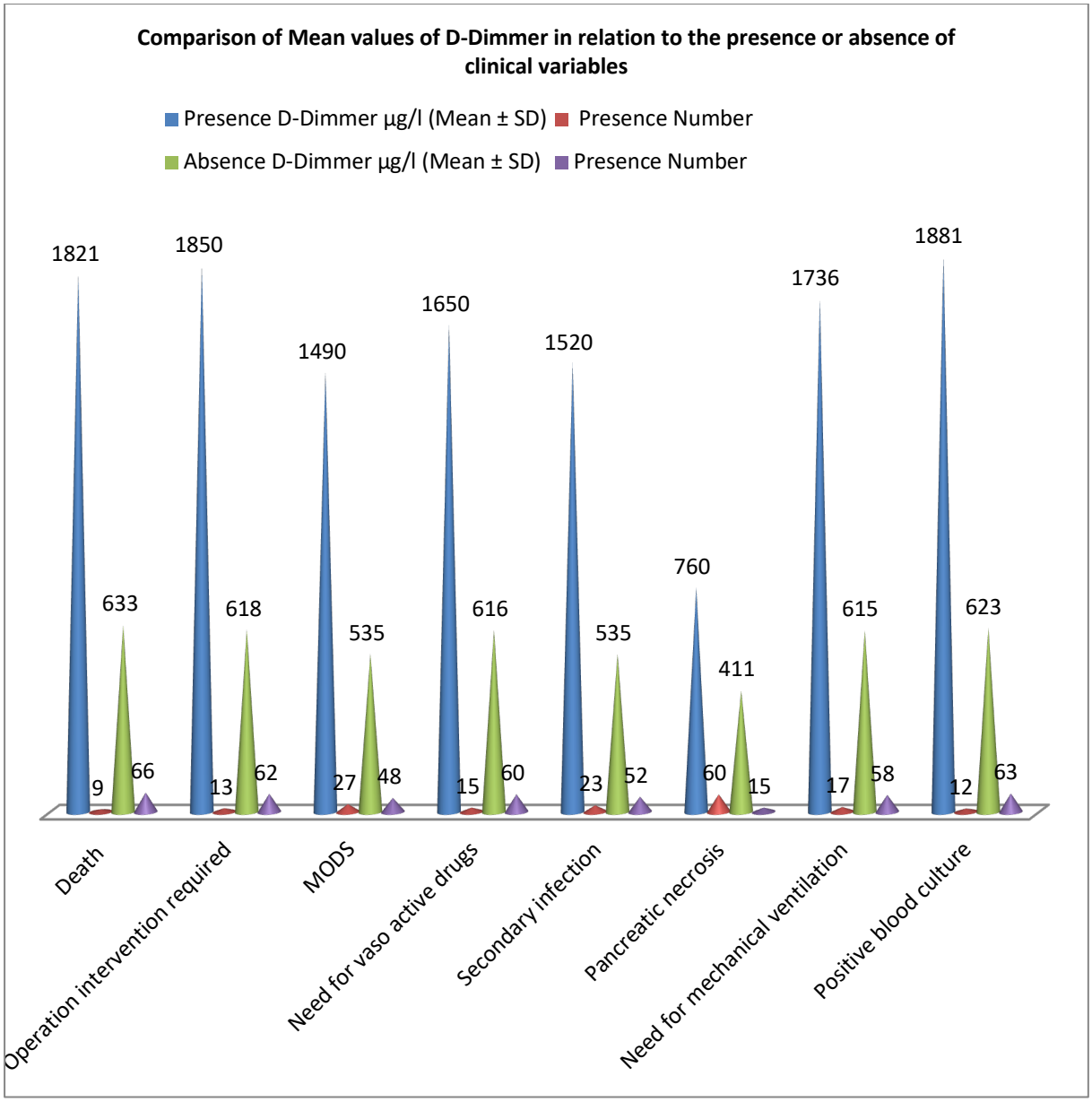


**Figure 3: Comparison of Mean values of D-Dimmer in relation to the presence or absence of clinical variables**

## Discussion

Present study of D-dimmer in severe acute pancreatitis in the Andhra Pradesh population Demographic data and clinical manifestations – 45 (60%) had biliary origin, 14 (18.6%) had alcohol use, 8 (10.6%) had hyperlipidemia, 8 (10.6%) had an idiopathic Apache-II score, and 9 (8.11) had a Ranson score.

48 hours after admission, 4 (3-6) CRP levels were 150 (103-201) in the Balthazar Index. 6 (5.7%) 95 (12%) hospitality mortality, 60 (80%) pancreatic, 23 (30.6%) pancreatic infection, 51 (68%) organ dysfunction, 27 (36%) MODS, 14 (18.6%) surgical intervention, 15 (9.5 to 25) duration of hospital stay; 10 (4 to 18) days of ICU (Table 1) Comparison of mean values of D-dimmer in relation to absence or absence of variables: death operation intervention required MODS, need for Vasoactive Drugs, Secondary Infection Pancreatic Necrosis, and need for Mechanical Ventilation Positive Blood Culture had a highly significant p value ($p<0.001$). These findings are more or less in agreement with previous studies [5,6,7].

The major difficulty in treating pancreatitis is predicting its severity. In the present study, it was proven that a D-dimmer test done on admission or within 24 hours after admission was valuable production. Apart from D-dimmer, many parameters like CRP, serum bilirubin, serum creatinine, uric acid, contrast-enhanced computed tomography (CECT), and the APACHI-II score also supported the elevations of D-dimmer.

D-dimmer is a fibrin degradation product (EDP), 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 [8]. D-dimmer, which is mostly used as an effective diagnostic tool to rule out deep venous thrombosis (DVT) and pulmonary embolism (PE), In addition to the thrombosis of the pancreas, pancreatitis leading to coronary venous thrombosis and splanchnic vein thrombosis has been reported [9].

The pathophysiology of AP has two components: systemic inflammatory response syndrome and pancreatic necrosis, which can be associated with infection and septic shock [10] SAP outcome or prognosis solely depends on the infection of pancreatic necrosis.

It is reported that there is a mild elevation of D-dimmer levels in patients with pancreatitis without complications, but with organic failure, the elevation of D-dimmer was seven times higher than normal. Elevated D-dimmer patients with MODs need surgical treatment in the presence of pancreatic necrosis and system involvement [11]

The etiopathology of elevated levels of D-dimmer is difficult to diagnose. The severity of pancreatitis depends on the extent of obstruction of pancreatic microcirculation due to microthrombi formation with fibrinolysis. Severe coagulative disorder suggested by a positive D-dimmer test is usually associated with an increased possibility of pancreatic necrosis and organ failure [12].

The D-dimmer levels affected by many factors, including pregnancy, inflammation, cancer, and surgery that increase fibrin production or breakdown, also increase D-dimmer levels. Consequently, the results available for one assay cannot simply be extrapolated to other assays, even those using similar formats.

**Summary and Conclusion**

The results of the present study demonstrate that D-dimmer measurement is a useful, easy, and inexpensive early prognostic biomarker of the evaluation and complications of SAP. The study requires that such clinical trials be carried out in hi-tech or super-specialty research centres with a large number of patients to confirm these significant clinical variables.

**Limitation of study**

Owing to the tertiary location of the research centre, the small number of patients, and the lack of the latest technologies, we have limited findings and results.

This research paper has been approved by the Ethical Committee of Andhra Medical College Hospital, Vishakhapatnam, Andhra Pradesh.

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