

## UTILITY OF THE PRODUCT VALUE OF SERUM ALBUMIN AND PROTHROMBIN TIME IN ASSESSING THE SEVERITY OF ACUTE PANCREATITIS

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### Abstract

**Background:** Acute pancreatitis (AP) is an inflammatory disorder characterised by local or systemic immuno-inflammation, which could lead to organ dysfunction and death. The present study aimed to study the utility of the product value of serum albumin and prothrombin time in assessing the severity of acute pancreatitis. **Materials and Methods:** This cross-sectional observational study was done in ESIC Medical College & PGIMSR, Chennai, for 18 months on 120 patients aged 20-75 years with acute pancreatitis without complications. The product value of serum albumin and prothrombin time were compared with the clinical severity, which was graded according to the APACHE II scoring system and compared with the clinical outcome. **Result:** Among 120 patients, the maximum of study participants was male, 119 (99.2%), and 41- 50 years (34.2 %). We found that around 23 (19.2 %) of the participants had a product value of < 35 (severe pancreatitis), 87 (72.5 %) of the participants had a product value of 35-70, and 10 (8.3 %) had a product value of more than 70. About 20 (16.7 %) participants had an Apache II score of more than eight, indicating severe pancreatitis. Further, 10 (8.3%) patients expired during the study. The sensitivity and specificity of the product value in severe pancreatitis are 90 % and 95 %, and the positive and negative predictive values are 78% and 97%, respectively. **Conclusion:** In conclusion, our present study reveals that the product value of serum albumin and prothrombin time on admission is independently associated with the severity of acute pancreatitis.

## INTRODUCTION

Acute pancreatitis (AP) is an inflammatory disorder characterised by local or systemic immuno-inflammation. It progresses from local pancreatitis to systemic inflammatory response, potentially leading to organ dysfunction and death. While some patients undergo a mild, self-limiting inflammatory process, others may develop a severe form of the disease with local or systemic complications, organ failure, and even death in advanced stages.<sup>[1]</sup> The severity of AP is classified into three levels according to the 2012 revised Atlanta classification: mild (without organ failure), moderately severe (with transient organ failure lasting less than 48 hours), and severe (with persistent organ failure lasting 48 hours or more).<sup>[2,3]</sup> Hence, it is crucial to promptly evaluate the disease's severity upon patient admission to determine appropriate therapeutic strategies. Effective treatments can significantly reduce mortality among

patients with severe pancreatitis.<sup>[4,5]</sup> Various invasive and non-invasive methods, including radiological imaging techniques, biochemical parameters, and scoring systems, are utilised for early diagnosis and assessment of AP severity. Currently, both serum albumin and prothrombin time (PT) are easily measurable. Although different examination methods may yield varying PT results, prothrombin time activity (PTA) can be a reliable means to standardise PT values.<sup>[6,7]</sup>

A significant decrease in serum albumin levels plays a crucial role in initiating the pathogenesis of AP. Hypoproteinemia has been observed in patients with AP, and extensive research has been conducted to investigate its underlying mechanism.<sup>[8,9]</sup> Coagulation dysfunction has also been identified in many AP patients. Markers such as Antithrombin III (APTT) levels and D-dimer have shown a strong association with the severity of AP.<sup>[10]</sup> The main aim of our study was to evaluate the utility of the product

value of serum albumin and prothrombin time in assessing the severity of acute pancreatitis.

## MATERIALS AND METHODS

This cross-sectional observational study was done in ESIC Medical College & PGIMSR, Chennai, for 18 months. The study was performed on 120 patients aged 20-75 with acute pancreatitis without complications. Institutional ethical committee approval and written informed consent was taken from all subjects before the start of the study.

### Inclusion Criteria

Patients aged 20 to 75 with acute pancreatitis without complications were included.

### Exclusion Criteria

Patients with chronic pancreatitis and pancreatitis with systemic disorders like hypertension, medical renal disease, and ischemic heart disease, and patients with pancreatic carcinoma and trauma-related pancreatitis were excluded.

Totally 120 patients attending general surgical OPD at ESIC hospital diagnosed with acute pancreatitis are admitted, and routine investigations are done along with serum albumin and coagulation profile. The product value of serum albumin and prothrombin time were compared with the clinical severity, which was graded according to the APACHE II scoring system and compared with the clinical outcome.

### Clinical Severity Assessment

The clinical severity of acute pancreatitis was graded using the APACHE II (Acute Physiology and Chronic Health Evaluation II) scoring system. This scoring system incorporates physiological parameters such as temperature, heart rate, blood pressure, respiratory rate, arterial blood gas values, and Glasgow Coma Scale (GCS) score, among others. The GCS score was assessed to evaluate the neurological status of the participants.

### Clinical Outcome Assessment

The clinical outcomes of the study participants were determined by monitoring their progress during the course of the study.

### Statistical Analysis

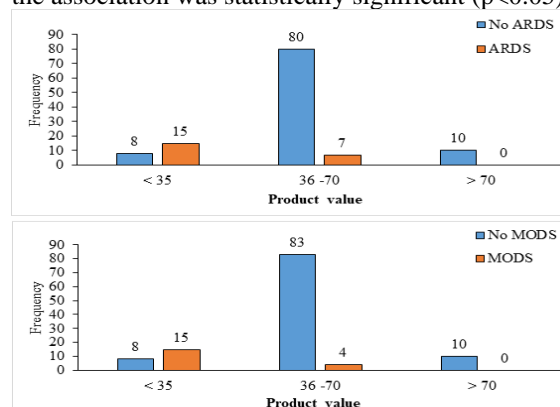
The collected data were entered into MS Excel and analysed using SPSS version 23.0. Descriptive statistics were depicted in frequency and percentage. The chi-square test was applied to find the association between variables, and a p-value less than 0.05 was considered statistically significant. Sensitivity, specificity, positive, and negative predictive values were calculated to determine diagnostic accuracy.

## RESULTS

Among 120 patients, male dominance was reported, and the maximum of study participants was 41- 50 years (34.2 %). The mean age of the study participants was observed to be  $42.5 \pm 10.0$  years. More than 112 (93 %) study participants had

tenderness, and 116 (96%) patients reported abdominal complaints. Around 82 (68.3 %) of the study participants had vomiting. The majority of the study participants had a GCS of 15/15 (78.3 %), followed by a GCS of 14/15 (16.7 %) and 13/15 (5%). Around 29 (24.2%) of the study participants were dehydrated, and Twenty percent of the study participants had abdominal guarding. Only 6 (5%) of the study participants had abdominal rigidity on examination. Around 8 (6.7 %) of the study, participants had an epigastric mass on examination. Most patients had no significant findings on chest x-ray, while 3 (2.5%) participants had pleural effusion on the right side. Around 10 (8.3%) study participants had dilated bowel loops on abdominal X-rays. The most common complication among the study participants is pseudocyst 10 (8.3%), followed by pancreatic necrosis 6 (5%) and pancreatic abscess 3 (2.5%). Of all patients, only 22 (18.3%) patients had acute respiratory distress syndrome (ARDS), and 19 (15.8%) had multiple organ dysfunction syndrome (MODS).

We found that around 23 (19.2%) of the participants had a product value of  $< 35$  (severe pancreatitis), 87 (72.5%) of the participants and a product value of 35-70, and 10 (8.3%) had a product value of  $> 70$ . About 20 (16.7%) participants had an Apache II score of more than eight, indicating severe pancreatitis. Further, 10 (8.3%) patients expired during the study. A higher proportion of ARDS was found among the participants with a product value less than 35 (severe pancreatitis), and the association was statistically significant ( $p < 0.05$ ). In addition, a proportion of MODS was found among the participants with a product value less than 35 (severe pancreatitis), and the association was statistically significant ( $p < 0.05$ ).



**Figure 1: Observation of (A) ARDS and (B) MODS against the product value**

A higher proportion of participants with an Apache II score of more than eight (Severe pancreatitis) was found among the participant with a product value of less than 35 (severe pancreatitis), and the association was found to be statistically significant ( $p < 0.05$ ). The sensitivity and specificity of the product value in severe pancreatitis are 90% and 95%, and the positive and negative predictive values are 78% and 97%, respectively.

**Table 1: Observation of various demographic and other variables of patients**

| Parameters           | Frequency (%) (N=120)           |             |
|----------------------|---------------------------------|-------------|
| Gender               | Male                            | 119 (99.2%) |
|                      | Female                          | 01 (0.8%)   |
| Age distribution     | 20 -30                          | 17 (14.2%)  |
|                      | 31- 40                          | 35 (29.2%)  |
|                      | 41- 50                          | 41 (34.2%)  |
|                      | 51 -60                          | 21 (17.5%)  |
|                      | > 60                            | 6 (5%)      |
| Mean age (Years ±SD) | 42.5 ± 10.0 years               |             |
| Tenderness           | Present                         | 112 (19.3%) |
|                      | Absent                          | 8 (6.7%)    |
| Abdominal pain       | Yes                             | 116 (96.7%) |
|                      | No                              | 4 (3.3%)    |
| Vomiting             | Yes                             | 82 (68.3%)  |
|                      | No                              | 38 (31.7%)  |
| GCS                  | 13/15                           | 6 (5%)      |
|                      | 14/15                           | 20 (16.7%)  |
|                      | 15/15                           | 94 (78.3%)  |
| Dehydration          | Adequate                        | 91 (75.8%)  |
|                      | Dehydrated                      | 29 (24.2%)  |
| Abdominal guarding   | Absent                          | 96 (80%)    |
|                      | Present                         | 24 (20%)    |
| Abdominal rigidity   | Absent                          | 114 (95%)   |
|                      | Present                         | 6 (5%)      |
| Epigastric mass      | Absent                          | 112 (93.3%) |
|                      | Present                         | 8 (6.7%)    |
| ARDS                 | Yes                             | 22 (18.3%)  |
|                      | No                              | 98 (81.7%)  |
| MODS                 | Yes                             | 19 (15.8%)  |
|                      | No                              | 101 (84.2%) |
| Product Value        | < 35                            | 23 (19.2%)  |
|                      | 35 -70                          | 87 (72.5%)  |
|                      | > 70                            | 10 (8.5%)   |
| Patient outcome      | Expired                         | 10 (8.3%)   |
|                      | Recovered                       | 110 (91.7%) |
| Apache II score      | > 8                             | 20 (16.7%)  |
|                      | < 9                             | 100 (83.3%) |
| Chest X-ray findings | NAD                             | 115 (95.8%) |
|                      | B/L Pleural effusion            | 1 (0.8%)    |
|                      | Right pleural effusion          | 3 (2.5%)    |
|                      | Mild pulmonary edema            | 1 (0.8%)    |
| Complications        | No                              | 100 (83.4%) |
|                      | Pancreatic abscess              | 3 (2.5%)    |
|                      | Pancreatic necrosis             | 6 (5%)      |
|                      | Pseudocyst                      | 10 (8.3%)   |
|                      | Pseudocyst, Pancreatic necrosis | 1 (0.8%)    |

**Table 2: Observation of ARDS, MODS and Apache II score to the product value**

| Product Value                 | ARDS                      |          | Total (%)                    | p-value |
|-------------------------------|---------------------------|----------|------------------------------|---------|
|                               | No (%)                    | Yes (%)  |                              |         |
| < 35                          | 8(8.2)                    | 15(68.2) | 23(19.2)                     | <0.05   |
| 36 -70                        | 80(81.6)                  | 7(31.8)  | 87(72.5)                     |         |
| > 70                          | 10(10.2)                  | 0(0.0)   | 10(8.3)                      |         |
|                               | MODS                      |          |                              |         |
| < 35                          | 8(7.9)                    | 15(78.9) | 23(19.2)                     | <0.05   |
| 36 -70                        | 83(82.2)                  | 4(21.1)  | 87(72.5)                     |         |
| > 70                          | 10(9.9)                   | 0(0.0)   | 10(8.3)                      |         |
| Apache II score               |                           |          |                              |         |
|                               | Severe pancreatitis (> 8) |          | No severe pancreatitis (< 9) |         |
| Severe pancreatitis < 35      | 18(90.0)                  | 5(5.0)   | 23(19.2)                     | <0.05   |
| No severe pancreatitis 36 -70 | 2(10.0)                   | 85(85.0) | 87(72.5)                     |         |
| No severe pancreatitis > 70   | 0(0.0)                    | 10(10.0) | 10(8.3)                      |         |

## DISCUSSION

Acute pancreatitis, particularly the severe form, is one of the gravest crises in the surgery department. Hypoalbuminemia and reduced PTA are commonly observed in liver dysfunction and can also be a cause or consequence of system inflammation response.

Arroyo et al. observed that as an effect of the inflammatory response, the consumption of albumin and coagulation factors increases. Still, the production is reduced, ultimately leading to hypoalbuminemia and PTA dropping.<sup>[11]</sup> These effects finally lead to Organ metabolism and

hemodynamics changes, creating a vicious circle, resulting in serious consequences and even death.

In our study, most patients were 41- 50 years (34.2%). The mean age of the study participants was observed to be  $42.5 \pm 10.0$  years. A similar age distribution is seen in a study by Hong et al., where the mean age of the study participants was 48 (IQR 37–63) years.<sup>[12]</sup> Whereas in a study by Vasudevan et al., the patients' mean (SD) age was 38.7 (15.5) years, less than other study observations.<sup>[13]</sup>

All the study participants except one are male (99.2%) in our study. Our observations contrast with studies done by Yang et al. and Li et al. Though there was striking male predominance in the above studies, almost 30% of the study participants were female.<sup>[10,14]</sup> More than 96% of the study participants complained of abdominal pain, and more than 93% had tenderness per abdominal examination. Around 68 % of the study participants had H/o vomiting, and the rest, 32%, had no complaints of vomiting. About 24% of the study participants were dehydrated, while 75.8% were adequately hydrated. According to Tenner et al, the rationale for early aggressive hydration in AP arises from this observation of frequent hypovolemia, which may occur due to numerous reasons, including vomiting, reduced oral intake, third spacing of fluids, increased respiratory losses, and even diaphoresis.<sup>[15]</sup>

In our study, twenty percent of the participants had abdominal guarding on examination, while the rest, 80%, did not. Only five percent of the study participants had abdominal rigidity on examination. Among the study participants, around 7% had an epigastric mass on examination. Similar to our study, in a study by Hong et al., the various etiology for severe acute pancreatitis was found to be majority biliary (42.7%).<sup>[12]</sup> Other causes were biliary and alcohol etiology, and few patients had combined biliary and hypertriglyceridemia etiology. The most important clinical feature was abdomen pain. A similar finding was seen by Li et al.<sup>[8]</sup>

In contrast to the above findings, Vasudevan et al. observed that though gallstones (45%) were the most common cause of AP, a few other important etiological factors were alcohol in 21%, idiopathic in 20%, post-ERCP in 11%, and miscellaneous causes in 3% of the cases.<sup>[13]</sup> Mayer et al. observed that early death is connected to the progress of severe and irreversible multiorgan dysfunction. In contrast, late death happens in the second phase of the illness, mostly due to sepsis and the consequences of organ failure.<sup>16</sup> Buter et al. further described that in addition to multiorgan dysfunction, the extent of pancreatic necrosis and septic complications are the major determinants of mortality in acute pancreatitis.<sup>[17]</sup>

Petrov et al. demonstrated that AP is an inflammatory disease, with mortality caused mostly by organ failure or infected pancreatic necrosis.<sup>[18]</sup> The most common complication among the study participants in our study is pseudocyst (8.3%), followed by pancreatic necrosis (5%) and pancreatic abscess

(2.5%). Vasudevan et al. observed Ninety-six (28%) patients in their research developed infective pancreatic necrosis leading to sepsis. In the present study, among the study participants, around 18% had acute respiratory distress syndrome, and around 16% had multiple organ dysfunction syndrome (MODS).<sup>[13]</sup>

In our study, a higher proportion of ARDS was found among the participants with a product value less than 35 (severe pancreatitis), and the association was statistically significant. ( $p < 0.00$ ). A similar finding was seen with a higher proportion of MODS among the participants with a product value  $< 35$  (severe pancreatitis), and the association was found to be statistically significant ( $p < 0.001$ ).

Vasudevan et al. observed that out of 343 patients, 170 (49.6%) had severe AP. Respiratory failure was the commonest organ failure recorded in their study. Several patients with respiratory failure alone were 100 (59%); respiratory failure with renal failure, 53 (31%); and respiratory and renal with cardiac failure, 17 (10%).<sup>[13]</sup> In their study, Li et al. demonstrated that the relation between organ failure and the product of serum albumin and prothrombin time on admission was shown to have an area under the curve (AUC) of 0.828 (95%CI: 0.783, 0.872), with a sensitivity of 54.2%, specificity of 96.9%. In terms of mortality, the AUC of the product of serum albumin and the prothrombin time was 0.905 (95%CI: 0.862, 0.948), even larger than that of Ranson, 0.887 (95%CI: 0.842, 0.933).<sup>[8]</sup>

Ning Yang et al. observed no statistically significant variance in prothrombin time or APTT between moderately severe and mild AP in biliary AP and hyperlipidaemic AP groups. Nevertheless, fibrinogen in the mild and moderately-severe hyperlipidaemic AP groups was suggestively higher than in the mild and moderately-severe biliary AP groups.<sup>[10]</sup> According to the observations made by Knaus et al., the APACHE system was formulated as a physiologically based arrangement model for estimating mortality in patients with a wide variety of illnesses in the critical care setting.<sup>[19]</sup> Chatzicostas et al. demonstrated that the APACHE investigators had established the APACHE III classification system. Though the new classification appears to be less precise than APACHE II in evaluating an array of consequences in patients with acute pancreatitis.<sup>[20]</sup>

In our study, a higher proportion of participants with an APACHE II score of more than nine (Severe pancreatitis) was found among the participant with a product value of less than 35 (severe pancreatitis), and the association was found to be statistically significant. ( $p < 0.05$ ). Similar observations were made by Mounzer et al. with a statistically significant value in APACHE-II ( $p < 0.0001$ ). The sensitivity and specificity of the product value in severe pancreatitis were found to be 90% and 95%, whereas the positive and negative predictive values were 78% and 97%, respectively.<sup>[21]</sup> From this study product value of serum albumin and Prothrombin time is observably reduced as the disease aggravated. This marker can

be used on the day of admission itself. Like the APACHE II score, we can easily predict the severity of the pancreas by this method.

## CONCLUSION

In conclusion, our present study reveals that the product value of serum albumin and prothrombin time on admission is independently associated with the severity of acute pancreatitis. We suggest that the product value of serum albumin and prothrombin time is a valuable tool for rapidly assessing the severity of pancreatitis in patients with AP. It will help to predict the severity and give early and vigorous treatment to prevent morbidity and mortality.

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