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*Original article*

# Outcome of Patients With Alcoholic Pancreatitis Admitted to Intensive Care Unit: A Single Center Experience

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## SUMMARY

**Background – While there is data on course and outcome of patients admitted with biliary pancreatitis, no study has assessed the outcome of patients admitted with alcoholic pancreatitis to intensive care units (ICU). Aims – To assess the outcome of alcoholic pancreatitis patients admitted to ICU. Methods – Prospective observational study of 37 consecutive patients with first episode of acute alcoholic pancreatitis admitted to ICU over a two year period. Data on patient characteristics and that required calculation of severity scores were collected. Patients were followed up to 30-days of discharge from ICU with 30-day mortality being the primary outcome measure. Results – Complications developed in 26 (70.3%) and necrosis in 23 (62.2%) patients. Six patients (16.2%) underwent pancreatic necrosectomy. ICU and 30-day mortality was 21.6% and 29.7%, respectively. On multivariate regression analysis, development of renal failure (adjusted odds ratio of 57.33, 95% CI: 2.77-1188.02, p=0.009) was significantly associated with 30-day mortality. Though all severity scores had comparable efficacy, SOFA score performed better with area under curve of 0.91 and 0.92 in predicting severity and 30-day mortality, respectively. Conclusions – Patients admitted to ICU with alcoholic pancreatitis may represent a distinct patient population with a high incidence of pancreatic necrosis. Development of renal failure is a vital prognosticator of mortality and SOFA score has good accuracy in predicting severity and mortality.**


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## INTRODUCTION

Acute pancreatitis (AP) is a common disease with a varied outcome ranging from mild sub clinical disease to an acute fulminant course. The etiological diagnosis of AP is crucial in patient management, as the disease course, management and outcome may vary according to the etiology.[1] Alcohol abuse and gall stones may account for about 80% of cases of AP, but their respective percentages may vary from country to country.[2] There is an increase in incidence of AP in the recent years,[3,4] with recent data suggesting this increase may be attributable to increase in alcohol consumption.[4] Although only 5% to 10% of alcoholics develop acute pancreatitis,[5] there is a lot of ambiguity regarding what increases a patient's susceptibility to get alcoholic pancreatitis.[6] Patients with alcoholic pancreatitis are generally men,[4] belong to younger age groups[4] and are considered to have a milder form of disease[7] but a majority of them may develop recurrent or chronic pancreatitis.[7-9] These patients may also be more prone to develop local complications like pancreatic pseudocysts or necrotizing pancreatitis.[10,11] While there is data on course and outcome of patients admitted with biliary pancreatitis,[12] no study has assessed the outcome of patients admitted with alcoholic pancreatitis in intensive care units (ICU). We aimed to assess the outcome of alcohol associated AP patients admitted to ICU.

## MATERIALS AND METHODS

This prospective observational study was conducted in patients with first episode acute pancreatitis, attributed to alcohol abuse, admitted to the ICU of a tertiary care hospital between December 2006 and November 2008. Di-

agnosis of pancreatitis was based on clinical presentation (acute abdominal pain associated with nausea and vomiting), laboratory parameters (increase in serum amylase at least to three times normal), and radiographic evidence with ultrasonography or computed tomography scan (inflamed edematous pancreas, cholelithiasis, choledocholithiasis, or biliary sludge). Patients with acute pancreatitis due to non-alcoholic causes (biliary, post-operative, drug induced, idiopathic), recurrent pancreatitis and acute exacerbation of known chronic pancreatitis were excluded from the study. Patients younger than 18 years were also excluded.

Day-one baseline patient characteristics and indication for ICU admission were recorded. The severity of illness was assessed by the Acute Physiology and Chronic Health Evaluation (APACHE) II,[13] III,[14] and simplified acute physiology *score* (SAPS) II[15] systems after the first 24 hours of ICU admission. Mortality probability models (MPM) $II_0$[16,17] were calculated from data obtained at time of admission. Organ dysfunction was assessed using the Sequential Organ Failure Assessment (SOFA)[18] score on day-one. The predicted death rate (PDR) was calculated based on the APACHE II and SAPS II scores. Modified Glasgow[19] and Ranson[20] scores were calculated by obtaining data up to 48 hours after admission.

Alcohol related disease was assumed if there was a clear history of alcohol consumption before the attack of pancreatitis and when no other identifiable factors could be identified. S*ystemic inflammatory response syndrome* (*SIRS*), sepsis, severe sepsis, and septic shock were defined according the American College of Chest Physicians/Society of Critical Care Medicine consensus conference.[21]

The primary outcome measure was 30-day mortality defined as death in ICU or within 30 days after discharge from ICU. Pancreatitis was defined as severe if it was associated with organ failure and/or local complications.[22] Organ failure was diagnosed according to the parameters included in the Atlanta criteria[22] with the presence of one or more of the following factors: shock (systolic blood pressure < 90 mm Hg), respiratory failure ($PO_2$ < 60 mm Hg), and renal failure (creatinine levels > 2 mg/dL after rehydration). Local complications included the development of pancreatic necrosis, abscess, or pseudocyst. All patients were followed up to 30 days after discharge from ICU or less if death had occurred earlier.

During the ICU stay, use of inotropes, mechanical ventilation (MV) or renal replacement therapy (RRT) were recorded. Finally, the lengths of stay in the ICU as well as total hospital stay were also recorded. Complications were classified as local (pancreatic necrosis, pseudocysts, abscess or fistula) and systemic (sepsis, and cardiovascular, respiratory, liver or renal failure).

The patients were managed conservatively, unless a complication had arisen, as per standard ICU protocols, with respect to resuscitation with intravenous fluids, use of antimicrobials, if there were signs of infection (empiric on admission, and then guided by microbiologic results), inotropes (if mean arterial pressure was < 55 mm Hg, in spite of fluid resuscitation), need for RRT (if serum creatinine was progressively increasing, with worsening of acidemia, with or without hyperkalemia), MV (if there was impending respiratory failure). Enteral feeding through naso-jejunal tube was preferred over parenteral feeding. Pancreatic necrosis, abscess, acute fluid collection, or pseudocyst were managed by either radiologically guided percutaneous fine-needle aspiration or surgery.

## STATISTICAL ANALYSIS

We used STATA version 9.0 (Stata Corp LP, College Station, Tex) for the statistical analysis. Potential factors associated with 30 day mortality were explored. The means of continuous variables were compared using students t-test and the medians were compared using a K - sample test for equality of medians. Categorical variables were compared using chi-square test or Fishers exact test as appropriate. Factors found significant in a univariate analysis were further explored in a multivariate model. A p value < 0.05 was considered significant for the analysis. The ability of scores to discriminate severity of pancreatitis and 30 day mortality were explored using Receiver Operator Characteristic (ROC) Curves and the Area under ROC curves (AUROC).

## RESULTS

A total of 37 patients admitted to ICU with diagnosis of alcohol associated acute pancreatitis were included in the study. The patient characteristics are given in Table 1.

The mean age of patients was 38.2 $\pm$ 9.1 (range 23 – 68). Complications developed in 26 patients (70.3%), 9 had local, 7 had systemic and 10 had both local and systemic complications. Thirteen patients (35.1%) required RRT out of which three (23.1%) received sustained low efficiency dialysis (SLED) and 10 (76.9%) received continuous renal replacement therapy (CRRT). Necrosis developed in 23 (62.2%) patients and six patients (16.2%) underwent pancreatic necrosectomy. Only one patient developed pseudocyst during the study period. Observed ICU and 30-day mortality was 21.6% and 29.7%, respectively.

**Table 1.** Patient characteristics, hospital course and outcome (n = 37)

| | |
|---|---|
| Mean age (median, years) | 38.2 ± 9.1 (38) |
| Sex (male/female) | 37/0 |
| Mean APACHE II ± SD (median) | 12.6 ± 8.4 (11) |
| Mean APACHE II PDR (median) | 20.1 ± 19 (12.9) |
| Mean APACHE III (median) | 48.1 ± 27.8 (43) |
| Mean SAPS II (median) | 29.6 ± 17.9 (26) |
| Mean SAPS II PDR (median) | 18.6 ± 24 (7.2) |
| Mean MPM $II_0$ (median) | 15.2 ± 19.2 (5.5) |
| Mean SOFA (median) | 6.3 ± 4 (5) |
| Mean Ranson (median) | 3.5 ± 2.1 (3) |
| Mean Glasgow (median) | 3 ± 1.4 (3) |
| Reason for ICU admission | |
| SIRS/Sepsis | 13 |
| Respiratory failure | 13 |
| Others* | 11 |
| Complications | |
| Local | |
| Necrosis | 8 |
| Necrosis + abscess | 1 |
| Systemic | |
| ACS | 1 |
| ARDS | 1 |
| Renal failure | 1 |
| Liver failure | 1 |
| MODS | 3 |
| Both | |
| Necrosis + MODS | 9 |
| Necrosis + MODS + pseudocyst | 1 |
| Mean ICU stay, days (range) | 7.5 ± 8.6 (1 – 32) |
| Mean hospital stay, days (range) | 13.5 ± 9.8 (2 – 40) |
| Necrosis | 23 (62.2%) |
| Severe pancreatitis | 26 (70.3%) |
| Renal support | 13 (35.1%) |
| Mean days on renal support (range) | 3.2 ± 6.3 (0 – 26) |
| Inotropic support | 13 (35.1%) |
| Mean days on inotropic support (range) | 3.4 ± 6.2 (0 – 20) |
| Ventilatory support | 14 (37.8%) |
| Mean days on MV (range) | 4.8 ± 9 (0 – 30) |
| Surgery | 6 (16.2%) |
| ICU – mortality | 8 (21.6%) |
| 30-day mortality | 11 (29.7%) |

**Others included 3 patients with severe abdominal pain, 2 each with uncontrolled hypertension and acute renal failure, and 1 each with diabetic ketoacidosis, atrial fibrillation, alcohol withdrawal and dyselectrolytemia. ACS – abdominal compartment syndrome, ARDS – adult respiratory distress syndrome, MODS – multiple organ dysfunction syndrome.*

On univariate analysis, ten factors were found to be significantly associated with 30-day mortality. These factors included – reason for ICU admission, development of renal or liver failure, length of ICU stay, need for MV, RRT or inotropic support, development of severe pancreatitis as defined by Atlanta classification, presence of necrosis and need for surgical intervention (Table 2). In a multivariate regression model that adjusted for factors significant in the univariate analysis, only development of renal failure (adjusted odds ratio of 57.33, 95% CI: 2.77-1188.02, p=0.009) was significantly associated with 30-day mortality.

Using ROC curves, all the scores showed comparable accuracy in predicting AP severity and 30-day mortality. Comparison of area under curve (AUC) data from the ROC analysis revealed that SOFA score most accurately predicted severity and 30-day mortality of alcoholic pancreatitis, AUC values, 0.91 and 0.92, respectively, although the difference between various scores was not statistically significant (Table 3).

## DISCUSSION

Patients with acute alcoholic pancreatitis admitted to ICU may represent a distinct sub-group of patients with varied disease course and outcome.[1] In our study, out of 37 patients admitted with alcohol associated acute pancreatitis in ICU, a great majority (70%) developed local or systemic complications, and 62% developed pancreatic necrosis out of which six patients required pancreatic necrosectomy. The observed ICU and 30-day mortality was 21.6% and 29.7%, respectively. Even though all severity scores had comparable efficacy in predicting severity and 30-day mortality, SOFA score performed better than the others.

In the early phase, severe AP causes release of inflammatory mediators which may further lead to SIRS and organ dysfunction.[23] This situation closely mimics organ dysfunction secondary to sepsis which generally supervenes in the late phase of the disease (usually after 14 days).[24,25] About one third of patients with AP may develop acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) which is a principle cause for early mortality.[26] Other causes for respiratory failure in AP may include pleural effusion, reduced diaphragmatic excursion due to severe pain, and basal atelectasis. Understandably, the common indications for ICU admission in our cohort were SIRS/sepsis and respiratory failure. Other causes for ICU admission included severe abdominal pain, uncontrolled hypertension, acute renal failure, dia-

**Table 2.** Univariate analysis for various parameters in predicting 30-day mortality

| Parameter of interest | Survivors (n = 26) | Non-survivors (n = 11) | P-value |
|---|---|---|---|
| **Age, years** | 37.2 ± 9.9 | 40.5 ± 6.6 | 0.33 |
| **Diabetes** | 8 | 4 | 1.00 |
| **Hypertension** | 14 | 4 | 0.48 |
| **Reason for ICU admission** | | | |
| **SIRS/Sepsis** | 5 | 8 | 0.003* |
| **Respiratory failure** | 10 | 3 | |
| **Others** | 11 | 0 | |
| **Renal failure** | 4 | 13 | 0.000* |
| **Liver failure** | 3 | 5 | 0.035* |
| **ICU stay, days** | 4.9 + 5.3 | 13.5 + 11.6 | 0.003* |
| **Hospital stay, days** | 12.8 + 7.4 | 15.4 + 14.2 | 0.47 |
| **Use of MV** | 3 | 11 | 0.000* |
| **Days on MV** | 14.3 + 8.1 | 12.4 + 11.7 | 0.79 |
| **Use of RRT** | 3 | 10 | 0.000* |
| **Use of inotropic support** | 3 | 10 | 0.000* |
| **Severe pancreatitis** | 15 | 11 | 0.015* |
| **Surgery** | 1 | 5 | 0.005* |
| **Presence of necrosis** | 13 | 10 | 0.027* |

**P-value < 0.05 was considered significant. ICU – intensive care unit, SIRS – systemic inflammation response syndrome, MV – mechanical ventilation, RRT – renal replacement therapy*

betic ketoacidosis, atrial fibrillation, alcohol withdrawal and dyselectrolytemia.

In an effort to determine which etiology causes most severe pancreatitis, Lankisch et al[11] discovered that patients with alcohol associated AP more frequently developed necrotizing pancreatitis and pancreatic pseudocysts. In addition, the need for artificial ventilation was also more in these patients as compared to AP patients with other etiologies.[11] Presence and extent of necrosis are independent risk factors for overall disease severity including organ failure and hence, ultimate outcome.[27-29] In the present study the majority of patients, 62%, developed pancreatic necrosis but only one patient (2.7%) developed pancreatic pseudocyst which is somewhat less than the reported incidence of pseudocysts after alcoholic pancreatitis, that is up to 10%. This may be explained by the fact that development of pseudocysts is a delayed complication of AP,[30] and the patients in our cohort were followed up to only 30 days after discharge from ICU.

Patients with alcoholic pancreatitis have a tendency to develop recurrent and chronic pancreatitis.[7-9] Alcoholic pancreatitis has been associated with low mortality rates, with figures of less than 10% reported in many studies.[7,31,32] However, these studies addressed mixed patient population admitted in both wards and ICU. In a large study, spanning over seven years with more than 70,000

**Table 3.** Area under curve (AUC) for predicting severity and 30-day mortality for various scoring systems

| Scoring system | AUC severity | 95% CI | AUC 30-day mortality | 95% CI |
|---|---|---|---|---|
| APACHE II | 0.81 | 0.66-0.95 | 0.89 | 0.75-1.00 |
| APACHE III | 0.78 | 0.62-0.93 | 0.85 | 0.70-1.00 |
| SAPS II | 0.88 | 0.76-1.00 | 0.89 | 0.79-0.99 |
| MPM $II_0$ | 0.84 | 0.71-0.97 | 0.90 | 0.80-1.00 |
| SOFA | 0.91 | 0.81-1.00 | 0.92 | 0.84-1.00 |
| Ranson | 0.83 | 0.68-0.97 | 0.88 | 0.77-0.99 |
| Glasgow | 0.90 | 0.81-1.00 | 0.85 | 0.73-0.97 |

AP patients, it was shown that the patients with alcoholic pancreatitis had the highest risk of dying.[3] As expected alcoholic pancreatitis patients admitted in ICU will have higher mortality rates. In our cohort where 70% of the patients had severe disease, the observed ICU and 30-day mortality was also higher, 21.6% and 29.7%, respectively. In patients with AP admitted to ICU, ICU mortality of 31% and hospital mortality of 42% has been reported in a large cohort of patients but in this study mortality according to etiological diagnosis was not cited.[33]

Development of organ failure and need for organ support in the form of MV, RRT or inotropic support have been shown to be predictors of poor outcome in patients with AP.[34,35] However, in the present study, only development of renal failure was found to independently predict 30-day mortality on multivariate regression analysis.

Prognostic scoring systems not only influence clinical decision making regarding therapeutic interventions and level of care required, but is also instrumental in predicting outcome in patients with AP. Traditionally, pancreatitis specific scores like Ranson and modified Glasgow scores have been utilized to predict outcome in AP with varying success rates.[12,33,36-38] A relative disadvantage of these scores is the need to collect patient data over the period of 48 hours. Although modified Glasgow score performed better than the Ranson score in our study, it was basically designed to identify severe AP and not to predict outcomes in severe AP which is also evidenced by higher AUC for predicting severity than for predicting mortality (0.90 vs 0.85).

General ICU scoring systems, especially APACHE II, have been extensively used and validated in patients with AP.[12,33,36,38] Even though it is more complicated to compute, it can be determined early in the disease course and have performed better than the pancreatitis specific scores.[33,38] MPM $II_0$ has rarely been evaluated as a score for predicting outcome in AP.[12] In a similar study conducted in patients with biliary pancreatitis admitted to ICU, it has shown better accuracy than the more frequently used APACHE II, III and Ranson scores with an AUC of 0.81 and 0.88 for predicting severity and mortality, respectively.[12] In our study too, it performed better than these scores with an AUC of 0.84 and 0.90 for predicting severity and mortality, respectively. Although computer assistance is required to calculate this score, it has an advantage that it can be computed immediately on admission.

The role of early-onset organ failure on the outcome of AP was first described by Isenmann[27] and was later substantiated in further studies.[39, 40] With increasing evidence in support of organ failure as a major factor determining outcome in AP, there is an increased emphasis on early recognition of the systemic aspects in terms of organ failure rather than determining local pathology in the course of AP.[41,42] Day-one SOFA score reflects early organ failure and hence, may better predict outcome in such patients. SOFA score has a highly reliable sensitivity and specificity and positive predictive value for the degree of severity of AP.[43] Our study added further credence to this fact, with SOFA score performing better than the other scores in predicting severity and outcome in alcoholic pancreatitis.

## LIMITATIONS

It was a single center retrospective study with a small cohort. All the patients in our study cohort were males which may not be representative of the disease prevalence in the community. This discrepancy may be due to higher prevalence of alcohol abuse among males in our society[44,45] and other studies with alcoholic pancreatitis have also shown male predominance.[31,46]

In conclusion, patients admitted to ICU with acute alcohol associated pancreatitis may represent a distinct patient population with a high incidence of pancreatic necrosis. Development of renal failure is a vital prognosticator of mortality and an organ failure assessment score like SOFA has got good accuracy in predicting severity and mortality in this sub-group of patients. Larger multicenter studies are warranted to further assess the course, outcome and predictors of adverse outcome for this subgroup of patients.

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