Validation of 'Moderately Severe Acute Pancreatitis' in patients with Acute Pancreatitis

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ABSTRACT

Introduction: Severe acute pancreatitis, according to Atlanta classification, is a heterogeneous group of patients with different outcomes. The patients with local complications and without organ failure have better outcome. This study has been conducted to determine the proportion of moderately severe acute pancreatitis and validate this subgroup in our population of patients.

Methods: A total of 172 patients with the diagnosis of acute pancreatitis were categorized into three groups according to presence or absence of local complications and organ failure as mild acute pancreatitis, moderately severe acute pancreatitis and severe acute pancreatitis and were compared in terms of need for intensive care unit care, length of ICU stay, need for intervention, length of hospital stay and mortality.

Results: Fifty seven (33%) were categorized as moderately severe acute pancreatitis. Need for ICU care (19.3% vs 100%, P< 0.001), length of ICU stay (1 vs 9.8 days, P< 0.001), length of hospital stay (8.3±3.7 vs 16.6±8.1 days, P< 0.001) and mortality (0% vs 33.3%, P< 0.001) between moderately severe acute pancreatitis and severe acute pancreatitis was significantly different. Moreover, mild acute pancreatitis and moderately severe acute pancreatitis had no mortality.

Conclusions: This study showed that moderately severe acute pancreatitis exists as a separate group different from mild acute pancreatitis and severe acute pancreatitis with no mortality as in mild acute pancreatitis.

Keywords: *moderately severe acute pancreatitis; Atlanta classification; outcome.*

INTRODUCTION

The 1992 Atlanta classification was proposed which is clinically based classification system that defines the severity and complications of acute pancreatitis (AP).[1] According to Atlanta classification, there are two groups: Mild acute pancreatitis (MAP) and severe acute pancreatitis (SAP). About 15-20% of patients with AP will have SAP characterized by high morbidity and mortality, prolonged hospital stay, and the need for intensive care. With the recent knowledge and concepts of course and pathophysiology of the disease and advancement in imaging techniques, several authors have pointed out various shortcomings in Atlanta classification.[2]

One of the main shortcomings of Atlanta classification is categorization of severity. Based on Atlanta classification, SAP comprises of heterogeneous group of patients having either both organ failure and local complications or just local complications. It has been found that the subgroup of patients with SAP having

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only local complications have high morbidity but low or no mortality as in case of MAP. The outcome of this group is different from those patients having organ failure as well as local complications. This subgroup of patients has been categorized as moderately severe acute pancreatitis (MSAP) who develop only local complications but no organ failure.[3] This new group of AP has been validated prospectively in several studies elsewhere, and have proposed to include this new subgroup in the revision of Atlanta classification.[4,5]

This study has been conducted to determine the proportion of MSAP in patients with AP and validate the subgroup in our population of patients.

METHODS

A prospective observational study was conducted in the Surgical Gastroenterology Units of Department of Surgery, Tribhuvan University Teaching Hospital, Kathmandu, Nepal over a period of 18 months. Approval from Department of Surgery of Institute of Medicine was obtained. Informed consent was taken from all the patients before enrolling into the study.

All patients with the diagnosis of AP who were ≥18 years of age were admitted from the Emergency Department after initial management either in the surgical ward or ICU. Those patients with organ failure at the time of the presentation in the Emergency Department were admitted in the ICU. All patients were managed aggressively with intravenous fluid, analgesics, and proton pump inhibitors. Severity was predicted using 11 point Ranson's criteria. All patients underwent USG of abdomen before being admitted in the Surgical Department.

During the hospital stay, those patients with SAP as per Atlanta classification underwent contrast enhanced CECT of abdomen after four days as per the UK guidelines for management of AP. Local complications were defined according to Atlanta classification and CTSI was calculated in all patients that underwent CECT abdomen. Organ failure was defined according to Marshall scoring system,[6] used for AP. The score of ≥2 for any organ was considered as organ failure provided that it persisted for >48 hours (persistent organ failure). Any organ failure that resolved within 48 hours was considered as transient organ failure.

The clinical course of all patients was recorded. The patients were categorized into three subgroups:

- SAP: presence of organ failure with/without local complications,
- MSAP: presence of local complications without organ failure and
- MAP: absence of organ failure/local complications.

Three groups were compared in terms of need for ICU, length of ICU stay, need for intervention, length of hospital stay and mortality.

Data was analyzed using SPSS version 11.5. Continuous variables was expressed as mean ± standard deviation and categorical variables as frequency tables and percentage forms. Independent t-test and chi square test was used to compare the data. The confidence interval of 95% was taken and p value <0.05 was considered as statistically significant.

RESULTS

A total of 172 patients with the diagnosis of AP were available for analysis. The demographic characteristics of the patients are given in Table 1. The mean age of patients was 42.7±16.5 years, with a male preponderance (55.2%). The most common etiology for AP was gallstones (60.5%), followed by alcohol (37.2%). Hypertriglyceridemia was found to be the cause of AP only in one patient. The incidence of idiopathic AP of this series was 22.1%. Overall mortality of the series was 2.3%.

Table 1. Patient demographic characteristics and etiology.

Variables	Frequency (n = 172) %
Age, year, mean ± SD	42.7 ± 16.5
Male	95 (55.2)
Female	77 (44.8)
Etiology	
Gallstones	104 (60.5)
Alchohol	64 (37.2)
Hypertriglyceridemia	1 (0.6)
Drugs	3 (1.7)
Idiopathic	38 (22.1)
Predicted severity	72 (41.9)
Local complications	68 (39.5)
Organ failure	12 (7)
Mortality	4 (2.3)

Total of 68 patients (39.5%) had local complications as defined by Atlanta classification (Table 2). The average CTSI in patients having local complications was 3.7. Out of 68 patients with local complications, 45 patients (66%) had acute fluid collection only, while 11 patients (16%) had >30% necrosis. The local complications

were graded according to CTSI.

According to Marshall scoring system for AP, 12 patients (7%) had persistent organ failure. The most common organ to fail was respiratory system in the form of ARDS in eight patients (42%), followed by cardiovascular in six patients (32%) and renal failure in five patients (26%). Further 11 patients (6.5%) had transient organ failure which was reverted back to normal after fluid resuscitation and oxygen supplementation. Fifty percent of the patients had two or more organ failure (Table 3).

Table 2. Types of organ failure.

Type of organ failure	n (%)
Transient organ failure	11 (6.4)
Persistent organ failure	12 (7)
ARDS	8 (42)*
Shock	6 (32)*
Renal impairment	5 (26)*
Single organ failure	6 (50)*
Multiorgan failure	6 (50)*

* Among patients with persistent organ failure (n = 12)

Table 3. Local complications (n = 68).

Type of complications	n %
Acute fluid collection	45 (66)
Fluid collection + necrosis < 30%	12 (18)
Necrosis 30-50%	7 (10)
Necrosis > 50%	4 (6)

The demographic characteristics and etiology was comparable between the three severity groups (Table 4). However, it was seen that females tend to have more mild disease. None of the patients in MAP required either ICU stay or intervention. There was no mortality in this group, and mean length of hospital stay was 4.9 ± 2.1 days. However, among patients with MSAP 11 out of 57 required ICU care. There was no mortality in this group and mean length of hospital stay was 8.7 ± 3.7 days. All patients with SAP were managed in ICU. However, none of the patients required any surgical or radiological intervention to manage the local complications. The mean length of hospital stay was 16.8 ± 8.1 days

MAP was found to be different from MSAP in terms of need for ICU, and length of hospital stay, which was statistically significant (Table 5). However, mortality was comparable between MAP and MSAP. Between MSAP and SAP, need for ICU stay, length of ICU stay and hospital stay, and mortality was found to be different which was statistically significant, $p < 0.001$. Similarly, MSAP is a separate entity from MAP having comparable mortality but significantly high morbidity, $p < 0.001$ (Table 6).

Table 4. Comparison of demographics and etiology between three groups.

Variable	MAP (n = 103)	MSAP (n = 57)	SAP (n = 12)	P value
Age (mean ± SD)	41.8 ± 16.6	43 ± 16.2	49.7 ± 17.6	0.29
Male, n (%)	49 (47.6)	39 (68.4)	7 (58.3)	
Female, n (%)	54 (52.4)	18 (31.6)	5 (41.7)	0.04
Etiology, n (%)				
Gall stones	57 (55.3)	39 (68.4)	8 (66.7)	0.24
Alcohol	33 (32)	25 (43.9)	6 (50)	0.21
Hypertrigly ceridemia	0	1 (1.8)	0	0.36
Drugs	3 (2.9)	0	0	0.36
Idiopathic	23 (22.3)	12 (21.1)	3 (7.9)	0.95

Table 5. Comparison of morbidity between MAP and MSAP.

Variable	MAP (n = 103)	MSAP (n = 57)	P value
Need for ICU stay, n (%)	0	11 (19.3)	0.001
Need for intervention, n (%)	0	0	NS
Length of ICU stay, mean ± SD, days	0	1	0.001
Length of hospital stay, mean ± SD, days	4.8 ± 2.1	8.6 ± 3.7	<0.001
Death , n (%)	0	0	NS

Table 6. Comparison between MSAP and SAP.

Variable	MSAP (n = 57)	SAP (n = 12)	P value
Need for ICU stay, n (%)	11 (19.2)	12 (100)	<0.001
Need for intervention, n (%)	0	0	NS
Length of ICU stay, mean ± SD, days	1	9.8 ± 4.6	<0.001
Length of hospital stay, mean ± SD, days	8.6 ± 3.7	16.6 ± 8.1	<0.001
Death, n (%)	0	4 (33)	<0.001

It has been shown that the proportion of MSAP in patients with acute pancreatitis was 33% and this group has been validated as an exclusive entity different from MAP and SAP. Surprisingly, none of our patients of acute pancreatitis required any form of intervention for the local complication during the study period.

DISCUSSION

Severity prediction in AP is very important so as to triage those patients requiring intensive care management. Atlanta classification has been used worldwide since 1992 to classify AP according to severity, taking morphological component into consideration. However, there have been various criticisms regarding Atlanta classification in severity stratification as there have been new insights and understanding in the pathophysiology of AP.[2,7]

SAP as described in Atlanta classification comprises a heterogeneous group of patients with local and systemic complications having different outcomes. Vege et al,[3] from Mayo Clinic, in a retrospective review of 207 consecutive patients with SAP, demonstrated that as compared to patients with organ failure, patients without organ failure had shorter hospitalization (28 vs 58 days, p = 0.02), less need for ICU care (50% vs 90%, p = 0.001), shorter time in ICU (5 vs 34 days, P<0.05) and decreased hospital mortality (2% vs 46%, P<0.01). Thus Mayo Clinic group have proposed that patients with local complications but without organ failure to be categorized separately as MSAP as this group have better outcome as those with organ failure. Accordingly, Talukdar et al,[4] in a prospective cohort of 137 patients with AP, demonstrated that 95 had MAP, 15 had SAP and 27 were categorized as MSAP. Similarly, de-Madaria et al,[8] from Spain, in their study to evaluate the three category classification as proposed by Vege et al, enrolled 144 patients with AP among which 91 had MAP, 11 had SAP and 42 were categorized as MSAP. In our study, among 172 patients, 103 had MAP, 12 had SAP and 57 were categorized as MSAP.

Talukdar et al,[4] showed that smaller proportion of patients with MSAP required ICU care (15% vs 80%, P<0.001). Whereas, E. de-Madaria et al,[8] showed in their cohort of 144 patients with AP, 2.4% of patients with MSAP required ICU as compared to 54.5% of patients with SAP (P<0.017). However, in our study, 19.3% of patients with MSAP required ICU which included surgical intensive care unit (SICU) also (19.3% vs 100%, P<0.001). The relatively increased number of patients being managed in ICU in our study may be due to the fact that we have also included management in SICU. However, the length of ICU stay in patients with MSAP was significantly less than those with SAP.

The low need of ICU care in the study by de-Madaria et al has been argued that the patients with predicted SAP could be managed optimally in semi-critical unit as well.

Length of hospital stay has been taken as one of the parameter to define morbidity. The patients with MSAP in the series of Tadulkar et al had relatively shorter median hospital stay as compared to those with SAP (6 days vs 21 days). However, the difference was not statistically significant (P = 0.06). While, patients with MSAP and SAP in de-Madaria et al series had similar prolonged hospital stay that was not statistically significant. In this study, patients with MSAP had length of hospital stay significantly less than those patients with SAP (8.5 ± 6.7days vs 16.6 ± 8.1 days, P < 0.001). Vege et al from the same group in their retrospective study have implicated increased pain requirements and difficulty in advancing their enteral feeds as the reasons for prolonged hospital stay. Similarly, de-Madaria et al in their study have also implicated need for nutritional support for prolonged hospitalization as 33.3% patients with MSAP required nutritional support in contrast to 2.2% with MAP. However, none of our patients with MSAP required nutritional support and increased need for pain requirement was not our concern. Therefore, although the length of hospital stay for MSAP was significantly higher than for MAP, it was also significantly less than that for SAP.

Talukdar et al in a prospective study confirmed that MSAP had no mortality as compared to those with SAP (0% vs 40%, P = 0.001). Similarly, de-Madaria et al also demonstrated no mortality in MSAP in contrast to 45.5% in SAP group (P < 0.017).This study had the similar findings in regards to mortality, none of the patients with MSAP died, while four out of 12 patients with SAP died during the hospital stay (0% vs 33.3%, p < 0.001). The mortality in SAP is very high and has been attributed to organ failure and pancreatic necrosis.

Various workers have shown that the early mortality due to progressive organ failure following development of SIRS due to local pancreatic inflammation accounts for 40-80% of all deaths due to AP.[9,10] In this series, there was four deaths all occurring within seven days of hospital admission and all had early and progressive organ failure. Among the four deaths, two had fluid collection only, one had fluid collection with necrosis < 30% and one just had diffuse enlargement of pancreas. None of the patients with > 30% necrosis develop organ failure and death, in contrast to the association shown by Garg et al between the extent and infection of pancreatic necrosis with organ failure and death in acute necrotizing pancreatitis.[11] In fact, few studies have shown that in the absence of organ failure, mortality from AP is negligible and presence of pancreatic necrosis does not necessarily correlate with organ failure.[12]

Our study reiterated the fact that having just two groups in severity classification as per Atlanta classification is not adequate. The third subgroup, MSAP having local complications without organ failure, as proposed by Vege et al, exists as an exclusive entity and has to be incorporated in the new classification. After completion of the draft of this manuscript two articles have been published regarding the severity classification. The PANCREA group has come up with determinant-based classification with four categories,[13] while acute pancreatitis classification working group,[14] has come up with three categories; both classification systems included the MSAP.

CONCLUSIONS

MSAP exists as an exclusive group different from MAP and SAP having both local complications and organ failure in terms of outcome. However, morbidity was not comparable to that of SAP as shown by other studies.

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