A STUDY ON RESPIRATORY COMPLICATIONS AND ITS OUTCOME IN ACUTE PANCREATITIS

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Abstract:

Background: Respiratory complications are frequent in acute pancreatitis, and respiratory dysfunction, presenting as Acute lung injury (ALI) or Acute Respiratory Distress Syndrome (ARDS), is a major component of multiple organ dysfunction syndrome (MODS), with a frequent need for ventilator support, which contributes to early death in severe acute pancreatitis. The current study was done with the objective of assessing the morbidity and mortality of acute pancreatitis cases with respiratory complications and to find out whether there is any association between the aetiology of acute pancreatitis and respiratory complications.

Methodology: It was a prospective observational study conducted in a tertiary care centre in Kerala. All participants admitted with symptoms suggestive of acute pancreatitis were screened for potential enrolment. The inclusion criteria employed were that the patients should be aged above 18 years, and presenting with the first episode of pancreatitis, irrespective of aetiology. All the patients who were admitted were monitored daily for the worsening of any respiratory complications and provided with adequate respiratory supports.

Results: Out of the 101 participants recruited, males were 84.2%. Mean (SD) age was 42.1 (11.4) years. Majority of cases (61%) had alcoholic aetiology. Fourteen patients required high flow nasal oxygen support, four patients were given face mask support, five patients required ventilator support and three patients required tracheostomy support. Respiratory complications and requirement of support were found to be associated with higher morbidity as well as mortality. Respiratory complications were higher in those with alcoholic etiology but this was not significant in univariate analysis.

Conclusion: Respiratory complications pose challenges in clinical course of acute pancreatitis in terms of morbidity as well as mortality. Aetiology did not seem to play a major role in development of respiratory complications.

Introduction:

The incidence of acute pancreatitis is in the range of 300 or more patients per million annually, with one-fifth of the patients suffering recurrent attacks.¹ Using the Atlanta classification on the severity, about 10% of acute pancreatitis patients are classified as severe.² Gallstones and alcohol account for 70-80 % of all acute pancreatitis etiologies, although acute pancreatitis may be the consequence of numerous etiologic factors. There have been differing reports with regard to whether etiologic factors affect clinical outcome and mortality of acute pancreatitis. Alcoholic etiology is reported to be most common in relapsing

cases, whereas gall stone etiology predominated in first attacks.³ Some studies have reported that biliary pancreatitis is more severe and is associated with higher mortality than alcoholic pancreatitis, whereas others noted higher complication with alcoholic.^{4,5} Mortality rates nearly double when there is necrotizing pancreatitis.⁶

Respiratory complications have been found to be common among patients presenting with acute pancreatitis in India, with hypoxemia at presentation pointing towards a higher risk of multi-organ failure during the course of treatment. The complications may range from pleural effusion with pulmonary infiltrates

to atelectasis, acute respiratory distress syndrome and respiratory failure.⁷ The pathophysiology of respiratory complications in acute pancreatitis is multi-faceted. During an initial phase, there will be exudation associated with alveolar damage, inflammatory response and microvascular injury, which is then followed by proliferative lung repair and fibrosis, mediated by various interleukins and different intermediary factors.⁸ These lead clinically to acute lung injury (ALI) and acute respiratory distress syndrome (ARDS).⁹

The severity of clinical course has been reported to be significantly higher among those with ALI, although the specific incidence might vary based on predisposing conditions.¹⁰ About one-third of all deaths from acute pancreatitis has been reported to occur prior to admission to hospital, and in most cases, is associated with ALI. Hospital deaths occur within the first week after admission in 35%-50% and the cause of death is related to single or multiple organ failure in a majority of cases. In elderly patients, up to 60% of all deaths within the first week are considered to be caused by pancreatitis-associated ALI and ARDS, while later deaths were attributed to other causes like infection.¹¹

There is a lacuna in Indian literature looking at the impact of respiratory complications on acute pancreatitis prognosis. The current study was done with the objective of assessing the morbidity and mortality of acute pancreatitis cases presenting with respiratory complications and to find out whether there is any association between the aetiology of acute pancreatitis and respiratory complications.

Methodology

The prospective observational study was conducted from January 2019 to June 2020 in the Department of General Surgery in a 1300 bedded private tertiary care centre in central Kerala, India, with the bulk of the patients hailing from districts of Thrissur, Palakkad, Malappuram and Ernakulam. All participants admitted with symptoms suggestive of acute pancreatitis were screened for potential enrolment. The inclusion criteria employed were that the patients should be aged above 18 years, and presenting with the first episode of pancreatitis, irrespective of aetiology. Patients with known respiratory disorders, known cases of chronic pancreatitis and pregnant women were excluded. The study was approved by the Institute Ethical Committee of JMMCRI, Thrissur.

Sample Size Calculation and Sampling

Based on the proportion of complications observed in an earlier publication, with 95% confidence level and 20% relative allowable error, minimum sample size comes to 43.¹² Consecutive sampling of all eligible cases admitted during the study period was done.

Data Collection and Follow Up

Once patients were identified, they were approached for written informed consent. All eligible and consenting participants were enrolled into the study. After noting the basic demographic characteristics and clinical details, patients were followed up to study outcomes. The diagnosis of acute pancreatitis was made on the basis of clinical symptoms and signs, and confirmed by a three times elevated lipase level or ultrasound of abdomen. They were classified into three categories – mild acute pancreatitis (no organ failure or any complications), moderately severe acute pancreatitis (organ failure that resolves within 48 hours and/or local or systemic complications without persistent organ failure) and severe acute pancreatitis (persistent organ failure of >48 hours and/or single/multiple organ failure as per the Revised Atlanta Classification 2012).¹³ Patients received standard treatment as per hospital protocols using analgesics and antibiotics for the severe pancreatitis along with naso-jejunal feeding or parenteral nutrition. All the patients with moderate to severe hypoxia, moderate pleural effusion or acute respiratory distress syndrome at the time of presentation or during follow up period were admitted in intensive care unit. All other patients with mild hypoxia or minimal to small pleural effusion were admitted in High dependency unit or step-down ICU. All other patients with stable vitals were admitted in male or female surgical wards. All the patients were followed up daily and were shifted to intensive care unit if patient develops worsening of respiratory complications.

The following laboratory measurements were obtained in all patients at admission: serum lipase levels, complete blood count, electrolytes, blood glucose, serum creatinine, liver function tests (AST, ALT, and bilirubin) and chest X-ray PA view. Arterial blood gas analysis were monitored daily if respiratory insufficiency occurs. Chest X-ray was repeated periodically as per clinical observations. Berlin's definition of Acute Respiratory Distress Syndrome was used to evaluate patients with clinical symptoms suggestive of ARDS.¹⁴

All the patients who were admitted were monitored daily for the worsening of any respiratory

complications and provided with adequate respiratory supports including face mask, high flow nasal oxygen, endotracheal intubation etc. Patients who developed respiratory complications were again monitored daily including their length of hospital and intensive care unit stay, need for the respiratory supports and their 30-day mortality during in hospital stay.

Statistical Analysis

Data were entered in Microsoft Excel 2016 and analysed using Statistical Package for Social Sciences (SPSS) version 25. Numerical continuous variables were expressed as mean and standard deviation if normally distributed and median and interquartile range if non-normal. Categorical variables were summarised in frequencies along with proportions and 95% confidence intervals. The association between various categorical variables was checked using Chi square test or Fischer exact test, as appropriate. Discrete numerical variables were compared using Mann-Whitney U test. Risk ratios were calculated for various independent variables using binomial logistic regression. A p value of <0.05 was considered as statistically significant.

Results

A total of 101 patients were admitted during the study period satisfied the inclusion criteria, and all of them consented to participate. Socio-demographic characteristics of the participants is shown in Table 1. The mean (SD) age of the participants was 42.1 (11.4) years. Males constituted 84.2% of the study sample. Diabetes and hypertension were the most common comorbidities at presentation. Two thirds of the patients presented with a history of alcohol use, which was reflected in the distribution of aetiology, shown in figure 1.

Clinical details of patients are shown in table 2. At admission, respiratory rate was the most commonly deranged parameter on examination, with 50% of patients being tachypnoeic. But spO₂ levels were normal for 86%. Around 36% of patients had elevated blood pressure and 32% had tachycardia. Endoscopic Retrograde Cholangiopancreatography (ERCP) followed by common bile duct sphincterotomy was done for six patients in the biliary pancreatitis group. Contrast enhanced CT scan was done in 44 patients out of which, pancreatitis was identified in 39 patients. Pancreatitis was identified in ultrasonography in 65

patients and there was no ultrasonographic radiological evidence of acute pancreatitis in the remaining. Patients also underwent laparoscopic cholecystectomy in the same hospitalization period. Computed tomography (CT) guided Malecot drainage of infected pancreatic fluid was done for one patient with alcoholic etiology. Left intercostal drainage was done for one patient with pancreatopleural fistula. There was no significant association between the existing co-morbidities and development of respiratory complications.

Out of 101 patients who got admitted with acute pancreatitis, recovery rate was 100% for the eight patients who required either face mask or nasal prongs for support and 92.9% for the 14 patients who required high flow nasal oxygen support. Five patients required ventilator support and out of which two patients (40.0%) got discharged and three patients (60.0%) expired. Three patients required tracheostomy and out of which one patient (33.3%) got discharged and two patients (66.6%) expired. The last two outcomes were statistically significant.

Rates of pleural effusion were higher in alcoholic etiology (30.6%) compared to biliary (20%) and others (13.8%). ARDS was found in 20% of patients of biliary etiology and closed to 7% in the other two. Five patients with alcoholic etiology developed atelectasis. Lung collapse was found in one patient of gall stone etiology whereas respiratory failure was found in one patient of alcohol etiology. But there was no significant association between etiology and type of respiratory complication. Etiology did not have any significant association with severity of pancreatitis or MCCU admission rates.

Morbidity indicators are given in table 3. Patients with respiratory complications were found to be at a higher risk of longer hospital stay and intensive care admission. Severity of pancreatitis and having an alcoholic etiology were also found to be significantly associated with respiratory complications. The overall mortality rate was 4.9%. Factors affecting mortality are discussed in table 4. Presence of any respiratory complication, requirement of any respiratory support, requirement of ventilator and requirement of tracheostomy were all found to be significant independent predictors of mortality in univariate analysis.

Table 1: Socio-demographic characteristics of patients presenting with acute pancreatitis to a tertiary care centre in Central Kerala, India (N=101)

Variable	Number of participants	95% Confidence Interval
Age Category (years)		
Less than 30	13 (12.9)	7.0 – 21.0
30 – 39	35 (34.6)	25.4 – 44.8
40 – 49	21 (20.8)	13.3 – 30.0
50 – 59	28 (27.7)	19.2 – 37.5
60 – 69	4 (3.9)	1.1 – 9.8
Sex		
Male	85 (84.2)	75.5 – 90.6
Female	16 (15.8)	9.3 – 24.4
Co-morbidities		
Type II diabetes mellitus	33 (32.7)	23.6 – 42.7
Hypertension	19 (18.8)	11.7 – 27.8
Coronary artery disease	5 (4.9)	1.6 – 11.1
Hypothyroidism	3 (3.0)	0.6 – 8.4
Chronic Kidney Disease	2 (2.0)	0.2 – 6.9
Arthritis	1 (1.0)	0.0 – 5.3
Behavioural Factors		
Positive history of alcohol use	61 (60.4)	50.1 – 70.0
Positive history of smoking	3 (3.0)	0.6 – 8.4

Figure 1: Aetiology of cases of acute pancreatitis presenting to a tertiary care centre in Central Kerala, India (N=101)**Table 2: Clinical Characteristics of those with acute pancreatitis to a tertiary care centre in Central Kerala, India (N=101)**

Variable	Number of participants, n (%)	95% CI
Presenting Complaints		
Abdominal Pain	99 (98.0)	93.0 – 99.7
Vomiting or Nausea	69 (68.3)	58.3 – 77.2
Fever	8 (7.9)	3.4 – 15.0
Constipation	6 (5.9)	
Loose stools	5 (4.9)	1.6 – 11.1
Breathing difficulty	5 (4.9)	1.6 – 11.1
Severity of Pancreas		
Mild	74 (73.3)	63.5 – 81.5
Severe	27 (26.7)	18.4 – 36.4
Respiratory complications		

Pleural effusion	25 (24.7)	16.7 – 34.3
ARDS	8 (7.9)	3.4 – 15.0
Atelectasis	5 (4.9)	1.6 – 11.1
Pneumonia	2 (2.0)	0.2 – 6.9
Lung collapse	1 (1.0)	0.0 – 5.3
Respiratory failure	1 (1.0)	0.0 – 5.3
PPF	1 (1.0)	0.0 – 5.3
Requirement of MCCU Admission		
Yes	27 (26.7)	18.4 – 36.4
No	74 (73.3)	63.5 – 81.5

Table 3: Association between respiratory complications and clinical morbidity (N=101)

Variable	Respiratory Complications		P value	RR	95% CI
	Present	Absent			
Alcoholic Aetiology					
Present	24 (39.3)	37 (60.7)	0.041*	1.9	0.9 – 3.9
Absent	8 (20.0)	32 (80.0)			
Severity of Pancreatitis					
Mild	10 (13.5)	64 (86.5)	<0.001*	6.0	3.3 – 11.0
Severe	22 (81.5)	5 (18.5)			
MCCU Admission, n (%)					
Required	21 (77.8)	6 (22.2)	<0.001*	5.2	2.9 – 9.3
Not required	11 (14.9)	63 (85.1)			
Days of Hospitalisation					
Range	3 – 27	2 – 17	<0.001**	-	
Median (IQR)	9.5 (7 - 13)	5 (4 - 6)			

*Chi square test

**Mann-Whitney U test

Table 4: Association between respiratory involvement and mortality (N=101)

Variable	Final Outcome		P value*	Risk Ratio	95% CI
	Discharged	Expired			
Respiratory Complications					
Present	28 (87.5)	4 (12.5)	0.034	8.6	1.0 – 74.1
Absent	68 (98.6)	1 (1.4)			
Respiratory support					
Required	20 (80.0)	5 (20.0)	0.001	-	-
Not Required	76 (100.0)	0 (0)			
Requirement of ventilator					
Present	2 (40.0)	3 (60.0)	0.001	28.8	6.1 – 135.3
Absent	94 (97.9)	2 (2.1)			
Requirement of tracheostomy					
Present	1 (33.3)	2 (66.7)	0.006	21.8	5.5 – 85.8
Absent	95 (96.9)	3 (3.1)			

*Fischer exact test

Discussion

Acute pancreatitis is a common disease entity with frequent occurrence and serious complications. While diagnosing a case of acute pancreatitis, a thorough history, physical examination, biochemical test and radiological evaluation are necessary. A hundred and one patients were enrolled in the current study, out of which 85 were males (84.2%) and 16 were females (15.8%) (M: F ~ 5.3:1). A prospective audit in 7 hospitals from South England (South England Audit) also showed males are commonly affected than females.¹⁵ Other studies also had a male predominance, the ration of M: F was low. This could be attributed to alcohol which is the major etiological agent in the study. In our study alcohol was the main etiological factor and was present in 61.4%. This result was comparable to a study by Pupelis G *et al.*¹⁶ Alcoholism was the main etiological factor in many other Indian studies, similar to ours.¹⁷ In contrast, in a study conducted in New Delhi, gallstones are found to be etiological factor in 49% of cases.¹⁸ Higher baseline alcohol consumption rates among the public could be the reason for the same. In our study, 27 patients (26.7 %) required MCCU care which is higher compared to other studies by Robert A Moran *et al* and Maryam Nesvaderani *et al.*^{19,20} Out of 27 patients 21 patients (77.8%) developed respiratory complications. So, a total of 21 patients out of 32 patients (65.6%) who developed respiratory complication required MCCU care. In our study, a total of 31.7% of patients developed respiratory complication which is comparable to study by Juneja *et al.*, but less compared to a study by Kaye and Takhar RP *et al.*²¹⁻²³ This could be again due to a reduction in the number of severe cases since some of them are referred to government medical college due to financial constraints. In our study 24.8 % patients developed Pleural effusion, 7.9% developed ARDS, 5% developed atelectasis, 2% developed pneumonia, 1% each developed lung collapse, respiratory failure and pancreatico-pleural fistula.

Out of 30 patients who required respiratory support, five patients required ventilator support and three required tracheostomies. Three out of five patients (60%) who required ventilator support and two out of 3 patients (66.6%) who required tracheostomy support expired which is statistically significant. All other patients who required other modalities of respiratory supports only like face mask, nasal prong, HFNO got better and got discharged. The mean duration of hospital stay in our study was 6.89 days which is

comparable to the other studies. But in patients who developed respiratory complication, it increased to 10.8 days. The mean duration of hospital stay of mild pancreatitis and severe pancreatitis cases were 5.24 days and 11.3 days respectively. Improvement in management have led to a significant reduction in mortality rates, particularly in specialized centres where technical resources and experienced personnel are available.²⁴ Around 80% of the mortality in our study was due to respiratory complication.

The overall mortality rate in our study was 5%, which is well below the recommended rate of 10 % by the U.K. guidelines.²⁵ The mortality rate of 5% in our study is comparable to the mortality in other studies.

The study has several strengths. Due to the prospective study design, the calculation of risk ratios was possible for various independent variables. Since all eligible cases from the specified study period were enrolled, there was no selection or sampling bias. The limitation of the study is that it was done at a single center and may be influenced by the treatment protocols being followed.

Conclusion

Those with alcoholic etiology might be at a higher risk of respiratory complications, even though co-morbidity status was found to be unaffected. Respiratory complications are associated with increased burden of morbidity and mortality among patients presenting with acute pancreatitis.

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