

A Study of Acute Kidney Injury in Severe Acute Pancreatitis in a Tertiary Care Hospital from South India

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Abstract: Acute kidney injury (AKI) is one of the serious complications in patients with severe acute pancreatitis (SAP). Severe acute pancreatitis is associated with a higher incidence of mortality ranging from 7% to 47% [1]. A tenfold increase in mortality has been shown to be observed in AP associated with acute renal failure [2]. **Objectives** (i) To identify the incidence of acute kidney injury in patients admitted with severe acute pancreatitis (based on revised Atlanta criteria-2012), (ii) To determine the severity of AKI in these patients based on the KDIGO-AKI-2012 criteria, based on urine output and serum creatinine elevation, (iii) To assess the mode of management and outcome of the renal dysfunction in these patients. **Methods:** This is a prospective cross sectional study of 100 patients, who were admitted in Govt. Stanley Medical College with severe acute pancreatitis diagnosed based on the Revised Atlanta classification (2012). The patients are followed up throughout the hospital stay and at least six months after discharge. The mode of management and the outcome of acute kidney injury were assessed. **Results:** Acute kidney injury occurred in 32 patients (32%). Majority of the Patients who developed AKI were alcoholic (78.13%). Mortality rate in our study was 12.5%. Mean age of patients who had acute pancreatitis was 42.92 ±12.60 years. There were higher proportion of diabetics in AKI group when compared to non-AKI group (40.63% vs 14.71%: p- 0.004). Stage 1 AKI was in 26 patients (81.25%), followed by stage 2 (n=4, 12.50%) and stage 3(n=2, 6.28%). Majority of the Acute Kidney Injury group patients were treated conservatively with fluids and antibiotics (n=30, 93.75%) and only 2 patients required hemodialysis (6.25%). Four patients expired (12.5%) in AKI group, while only one patient expired in non-AKI group (p- 0.018). The risk of death in SAP with AKI patients with Diabetics is 1.62 times significantly more than patients with non-diabetics (p- 0.0074). In SAP with AKI patients the risk of death significantly increases with alcohol intake, serum amylase >200 IU/L, serum creatinine >2.4mg/dl at admission and when AKI stage >1 at admission (odds ratio: 3.04; 3.58; 4.29; 3.59). **Conclusions:** In our study, the incidence of AKI in severe acute pancreatitis patients was 32%. Based on the KDIGO staging of acute kidney injury, majority of the patients were in stage-1. Diabetes mellitus and ethanol use were significantly related with the development of AKI. Most of them recovered with conservative management and only 2 patients required dialysis support. An early recognition of AKI in acute pancreatitis and timely management can improve the outcome and reduces mortality.

Keywords: acute pancreatitis, acute kidney injury, serum amylase.

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I. Introduction

Pancreatitis is an inflammatory process where pancreatic enzymes auto-digest the gland. Acute pancreatitis can be classified as mild (interstitial) pancreatitis and severe (necrotizing) pancreatitis. In severe acute pancreatitis (SAP), there is necrosis of the gland and spread of inflammatory process outside the gland. Gall stones (40- 50%) and alcohol (30-40%) account for the majority of cases [1]. Acute kidney injury (AKI) is one of the major complications that occurs in patients with acute pancreatitis due to many factors like pre-renal azotaemia, septic shock, increased intra-abdominal pressure and abdominal compartment syndrome [2].

In acute pancreatitis, there is peri-pancreatic fluid sequestration, which causes reduction in extra cellular fluid (ECF) volume and intravascular volume, which results in decreased renal perfusion and glomerular filtration rate leads to pre-renal acute kidney injury. Phospholipase A2 (PLA2) released from recruited polymorphonuclear cells gets deposited in the tubular cells of kidney resulting in cell death either by apoptosis or via necrosis. In acute pancreatitis systemic inflammation occurs which increases the vascular permeability leading to accumulation of fluid in the peritoneal cavity and extraperitoneal space, which is of exudative in nature. This results in the increase in the intra-abdominal pressure and thereby leading to intra-abdominal hypertension. This resultant raised intra- abdominal pressure decreases the renal perfusion and

causes pre-renal AKI [3]. Thrombotic microangiopathy as a result of acute pancreatitis is observed in certain number of patients. Secondary infection of the necrotic tissue in necrotising pancreatitis is noted in 40–70% of patients. In such scenarios, mortality rate raises upto 50% due to sepsis and multi organ dysfunction syndrome (MODS) [4].

Systemic inflammatory response syndrome (SIRS) is a common complication of severe acute pancreatitis. Various inflammatory mediators (cytokines and increased nitric oxide synthesis) are released into the systemic circulation. This causes systemic vasodilatation and stimulation of baroreceptors, resulting in increased sympathetic activity and angiotensin production which ends up in reduction in glomerular filtration rate (GFR) & multiple organ dysfunction. Hence it is observed that vasoconstriction, inadequate perfusion, and hyperviscosity of blood leads to hypoxia and thereby development of AKI in patients with acute pancreatitis [5, 6, 7].

II. Objectives

1. To identify the incidence of acute kidney injury in patients admitted with severe acute pancreatitis (SAP).
2. To determine the severity of acute kidney injury in these patients based on the KDIGO-AKI-2012 criteria, (urine output and the serum creatinine elevation).
3. To assess the mode of management and outcome of the renal dysfunction in these patients.

III. Patients And Methods

This study was a prospective cross sectional study done in 100 patients admitted in Department of Medical & Surgical gastroenterology, Govt. Stanley Medical College with severe acute pancreatitis from January 2015 to June 2016. Pancreatitis confirmed by the presence of two among the following three criteria in patients.

1. Abdominal pain strongly suggestive of pancreatitis
2. Serum Amylase or Lipase activity at least 3 times greater than the upper limit of normal.
3. Characteristic finding of acute pancreatitis on trans-abdominal ultrasound scan or CT scan.

Patients were diagnosed to have severe acute pancreatitis (SAP) based on the Revised Atlanta classification - 2012 (organ failure >48 hours/ CT evidence of severe necrosis, more severity grading in RANSON'S or APACHE II score). Patients who has chronic pancreatitis presenting with acute severe pancreatitis, Patients with known CKD and post-surgical pancreatitis, trauma, inflammatory bowel disease, were excluded from the study. Pulse, blood pressure, urine output, blood urea, serum creatinine, blood sugars, liver function test, serum calcium and complete blood count checked for all patients. Patients with AKI were identified based on the KDIGO-AKI-2012 guidelines and staged accordingly. The patients are followed up throughout the hospital stay and atleast six months after discharge. The mode of management and the outcome of acute kidney injury were assessed.

IV. Data Analysis

Descriptive statistics was done for all data and were reported in terms of mean values and percentages. Suitable statistical tests of comparison were done. Continuous variables were analysed with the unpaired t test. Categorical variables were analysed with the Chi-Square Test and Fisher Exact Test. Statistical significance was taken as $P < 0.05$. The data was analysed using SPSS version 16 and Microsoft Excel 2010.

V. Results

Table no 1: Demographic characteristics of the patients

Patient data	SAP with A.K.I.(n=32)	SAP without A.K.I.(n=68)	P value
Age ,mean+/-S.D.	41.97+/-11.26	43.87+/-13.93	0.4694
Diabetes mellitus	13	10	0.0041
Hypertension	4	13	0.5706
Alcohol	27	50	0.0355
Smoking	20	36	0.3690

A total of 100 severe acute pancreatitis patients were followed up. Acute kidney injury occurred in 32 patients (32%). Mean age of patients who had acute pancreatitis was 42.92 ± 12.60 years. No significant difference seen between the patients with AKI and patients with no AKI in terms of age (p 0.47) [Table 1]. Majority of the Patients who developed AKI were alcoholic -25 patients (78.13%), followed by carcinoma pancreas -3 patients (9.38%), Cholelithiasis -2 patients (6.25%) Carcinoma of gallbladder and Sepsis 1 patient each (3.13%).

Table no 2: Clinical profile of the patients

Data ,mean+/-S.D.	SAP with A.K.I.(n=32)	SAP without A.K.I.(n=68)	P value
S. amylase IU/L	931.84+/- 920.89	595.93+/- 998.12	0.1025
S.lipase IU/L	633.63+/- 312.65	556.06 +/- 762.83	0.4734
S.creatinine.mg/dl			
At admission	2.57 +/-1.35	0.96+/- 0.24	0.0000
Peak value	2.88+/- 1.32	1.12+/-0.21	0.0000
At discharge	1.53+/- 0.66	0.93+/- 0.15	0.0000
Urine output			
At admission	1081.25+/- 183.93	1283.82+/-241.02	0.0000
Nadir	765.63+/- 228.05	1150.00+/-169.72	0.0000
At discharge	1370.00+/-196.78	1523.53+/-246.24	0.0016
Mortality	4 (12.5%)	1(1.5%)	0.0182

There were higher proportion of diabetics in AKI group when compared to non-AKI group (40.63% vs 14.71%). This difference was statistically significant (p value is 0.004). Eventhough alcohol was important factor in both in AP with AKI (84.34%) and AP without AKI (73.53%) groups, AP with AKI group has statistically significantly higher percentage of alcoholics than AP without AKI group (p value 0.035). [Table 1]

Majority of the severe acute pancreatitis with Acute Kidney Injury group patients had stage 1 AKI according to the KDIGO guidelines. (n=26, 81.25%), followed by stage 2 (n=4, 12.50%) and stage 3(n=2, 6.28%). Majority of the Acute Kidney Injury group patients were treated conservatively with fluids and antibiotics (n=30, 93.75%) and only 2 patients required hemodialysis (6.25%). Four patients expired (12.5%) in AKI group, while only one patient expired in non-AKI group (p- 0.018). [Table 2]

The risk of death in SAP with AKI patients with Diabetics is 1.62 times significantly more than patients with non-diabetics (p- 0.0074). In SAP with AKI patients the risk of death significantly increases with alcohol intake, serum amylase >200 IU/L, serum creatinine >2.4mg/dl at admission and when AKI stage >1 at admission (odds ratio: 3.04; 3.58; 4.29; 3.59). [Table 3]

Table no 3: Multivariate analysis of variables with risk of death.

Independent Variables	Death Ratio		
	Old Ratio	95% Confidence Interval	P Value
Age <50 years	3.73	0.18 -77.18	0.3924
Diabetes Mellitus	1.62	0.56-3.84	0.0074
Hypertension	1.55	0.18-12.64	0.6848
Alcoholic	3.04	1.33-6.95	0.008
Smoking	5.36	0.48-59.92	0.173
Serum Lipase > 300 U/L	1.10	0.86-1.41	0.062
Serum Amylase > 200 U/L	3.58	1.15-11.13	0.018
Serum Creatinine > 2.4 mg/dl	4.29	1.12-16.52	0.039
Urine Output < 400 ml/day	1.91	0.33-38.4	0.216
Staging > 1	3.58	1.15-11.13	0.043
Haemodialysis Treatment	1.161	1.17-12.49	0.061

VI. Discussion

Acute kidney injury occurred in 32% of our severe acute pancreatitis patients. Various literatures states that the incidence is 14 to 42% [8-12]. However higher incidence of AKI was noted in our study when compared to the study by Kumar et al from central India in which the incidence of AKI in SAP patients was 19.4%. The mortality rate among AKI group in our study was 12.5%. This is in contrast to the study by Hung-Yuan Lin et al [13] and study by Ravindra Kumar et al [14] in which the mortality rates were higher (23.76% & 57.1%).

Majority of the Patients who developed AKI in our study were alcoholic -25 patients (78.13%) followed by carcinoma pancreas-3 patients (9.38%), Cholelithiasis -2 patients (6.25%). In study by Ravindra Kumar et al from central India, the cause of pancreatitis was alcohol intake in 24 patients (33.33%), cholelithiasis in 18 patients (25%). Majority of the SAP with AKI group patients in our study had stage 1 according to the KDIGO guidelines (n=26, 81.25%), followed by stage 2 (n=4, 12.50%). In the study by Jiaojiao Zhou et al [15] majority were AKIN stage III 34.3% followed by AKIN stage II 18.4%. Patients with AKI had significantly higher mortality when compared to non-AKI SAP group (12.5% vs 1.5%; p- 0.0182).

Prognosis of the SAP patients with AKI is influenced by presence of diabetes, alcohol use, severity grading of AKI and the severity of acute pancreatitis. These findings were in concordance with the study by Ravindra Kumar et al.

VII. Conclusion

In this study, one third of patients with severe acute pancreatitis developed acute kidney injury meaning that patients with acute pancreatitis has very high risk of developing AKI. Diabetes mellitus and ethanol use were significantly related to the development of AKI. Presence of AKI and higher grades of AKI were associated with worse patient outcomes. Early identification of AKI and timely management may improves the outcome in acute pancreatitis.

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Declaration of Interest

This study had no specific funding source. All authors declare no conflicts of interest for this work.

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