Research Article

AN OBSERVATIONAL PILOT STUDY TO DETERMINE FACTORS PREDICTING SURVIVAL AND MORTALITY IN ACUTE PANCREATITIS

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A R T I C L E   I N F O

A B S T R A C T

Introduction: Acute Pancreatitis involves a rapid inflammatory cascade leading to parenchymal injury. 80-90% of cases are self limiting while the rest lead to a much severe form of disease. Despite strict protocols and various markers of pancreatitis, it has a high mortality rate. This pilot study is a small scale test of the methods and procedures to be used on a larger scale for evaluating clinical, biochemical and radiological parameters that predict need for intervention, morbidity and mortality.

Methodology: This Pilot study took place in a tertiary care hospital among 50 patients of acute pancreatitis for one year. Various clinical parameters were used to identify severity of disease. Ranson's score was used to access biochemically demonstrated severity and CT severity score to access radiological severity.

Results and Discussion: Out of 50 patients 38 were male with average age of 31-50 years and 78% were alcoholic. 80% patients had Systemic Inflammatory Response Syndrome. Ranson Score at admission greater than 3 was only 2% which increased to 10% after 48 hours. 18 patients required intervention viz percutaneous drainage, ERCP, or surgery.

Conclusion: Acute pancreatitis was more common in alcoholics and male gender. There was no significant association between Ranson Score and need for intervention (p=0.23). Ranson Score and CT Severity score had no statistical significance in predicting mortality (p=0.48, p=0.11). Detailed analysis was not done from the pilot study as the small sample size had already proved that there were no statistically significant findings with the given parameters. The study design however proved to be feasible for a larger study of 100 patients. This was the main reason behind conducting this pilot study with hope to work on larger data from the final study.

INTRODUCTION

Acute Pancreatitis is a rapidly progressive inflammatory disorder, developing from a complex cascade of immunological events. It ranks within the 15 most fatal illnesses worldwide despite standardised treatment protocols. Abnormal premature activation of digestive enzymes within pancreatic acinar cells is a critical initiating event resulting in autodigestion of pancreatic parenchyma.

Acute Pancreatitis can be primarily diagnosed based on the following factors:

1. Epigastric pain of acute onset (which often but not always radiates to the back)
2. Serum lipase and/or amylase levels more than 3 times normal.

Contrast enhanced abdomen CT no longer plays a pivotal role in diagnosis but is a means of defining patients without any definitive diagnosis or those who are non responsive

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irrespective of treatment. CT is however useful in guiding minimally invasive interventions for complicated cases. CT severity index also indicates severity of disease.

Irrespective of the etiology, the course of disease can range from mild self limiting to severe life threatening disease. Severe acute pancreatitis is characterized by persistent organ failure with or without one or more local and/or systemic complications. Acute pancreatitis is managed initially by three pillars consisting of fluid resuscitation, pain control and nutritional support. Patient is kept NPO for a period of time to facilitate pancreatic rest. While mild cases respond severe cases often require additional care viz antibiotic cover, ERCP in biliary pancreatitis and prolonged enteral feeding. Secondary infected necrosum requires intervention in the form of minimally invasive, laparoscopic or open necrosectomy.

Fruitful patient management consists of accurate diagnosis, swift medical management and timely surgical intervention. Foresight into those patients whom will require additional resources is key in the adequate management of pancreatitis. Serum markers namely CRP, hematocrit and trypsinogen

activated peptide and IL - 6 have promising evidence of determining severity of disease. Despite strict protocols, pancreatitis remains as one of the most those diseases with a stellar complication rate. This pilot study is a small scale test of the methods and procedures that predict need for intervention, morbidity and mortality of Acute Pancreatitis.

MATERIAL AND METHODS

This Pilot study was conducted in our hospital for a period of one year from June 2012 to November 2013. 50 cases of acute pancreatitis treated in this tertiary care centre were observed. Clinical parameters used to identify severity were temperature, pulse, respiratory rate and WBC counts. Ranson's score (3 and above) was used to access biochemically demonstrated severity and CT scan to access radiological severity. (Modified Balthazar's score >6).

Inclusion Criteria

1. 18-70 Years of Age
2. Males and Females
3. First time presentation to our institute.
4. First episode of pain.

Exclusion Criteria

1. Chronic Pancreatitis
2. Acute on Chronic Pancreatitis
3. Patients transferred from other health care facilities
4. Patients presenting after day 5 of Pain Onset; or after intervention.

The salient features studied in all patients were:

1. Clinical parameters and signs
2. Ransons score at Admission and after 48 hours
3. Serum Amylase and Lipase.
4. CT findings on the 5th day of pancreatitis and use of Modified Balthazar's score to grade severity.
5. Any intervention during the first admission: Surgical or Radiology-guided.
6. Any complications that occurred.

RESULTS

Out of 50 patients thirty-eight (76%) patients were male and 12 (24%) were female [Figure 1]. One patient was below 20 years of age, 12 patients between 21 to 30 years, 14 patients each were between 31 to 40 years and 41 to 50 years of age, 6 were within 51 to 60 years and the rest beyond 60 years of age [Figure 2]. The mean age was 40.5 years.
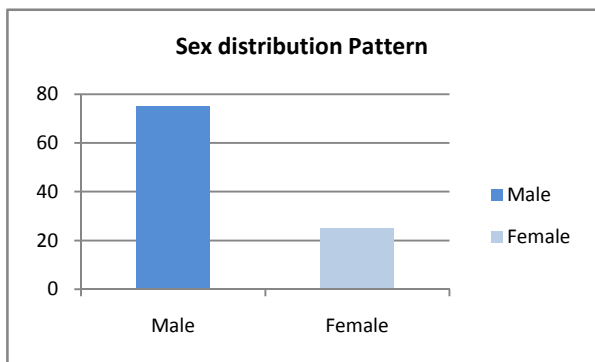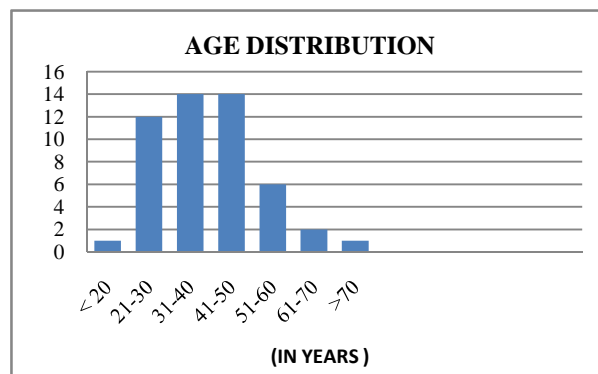

Fig 1 Gender distribution

Fig 2 Age distribution

34 (78%) patients had a history of alcohol intake and they were all male. Eleven patients suffered from gall stone induced pancreatitis of which 8 (16%) were females. No etiology could be found in the remaining 5 patients of whom four were women. These patients were labeled as having idiopathic pancreatitis [Figure 3].
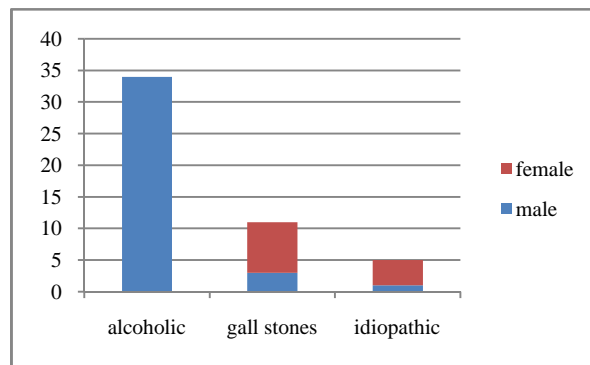

Fig 3 Etiology

In our study, on clinical examination we found that, 16 out of 50 patients had a temperature of >38 C [Figure 4].
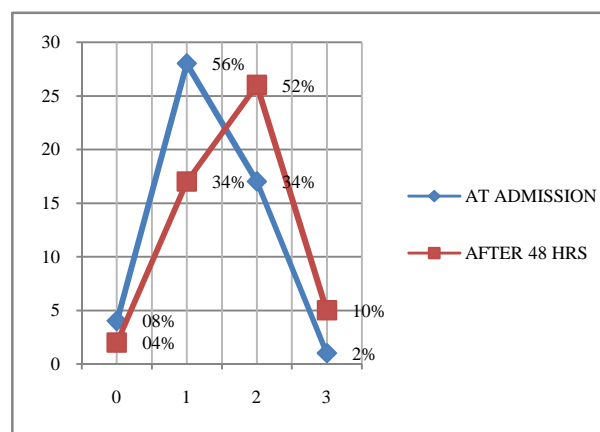
Fig 4 The above graph represents Ranson's criteria at the time of admission and after 48 hours of admission of patient

Forty five (90%) patients had a pulse above 90 per minute. (Figure 5) 44 (88%) had a respiratory rate more than 18 per minute (Figure 6). Thirty nine (78%) had counts raised beyond 12000 per cumm. (Figure 7) Eleven (22%) patients had a raised alkaline phosphatase levels, 36 (72%) had raised LDH and 6 (12%) patients had raised SGOT levels. BUN was raised in 14 (28%) of patients. Out of a total 50 patients, 40 (80%) had Systemic inflammatory response syndrome (Table

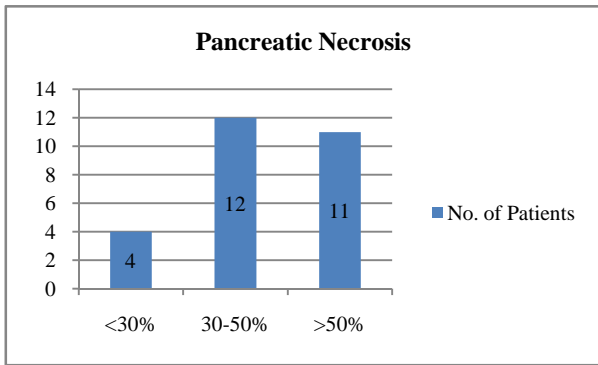1). Lipase levels greater than twice normal were seen in 96% patients [Table 2].
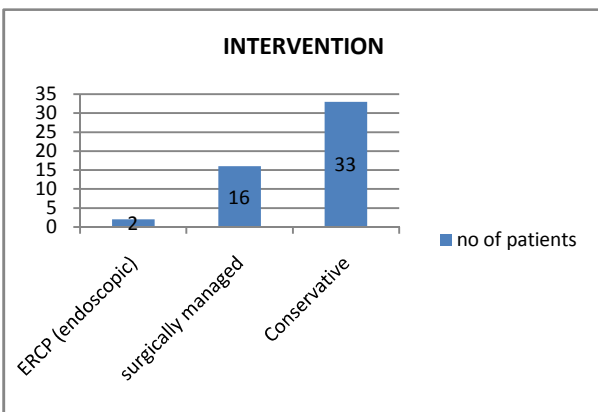

Fig 5 Distribution of extent of Necrosis

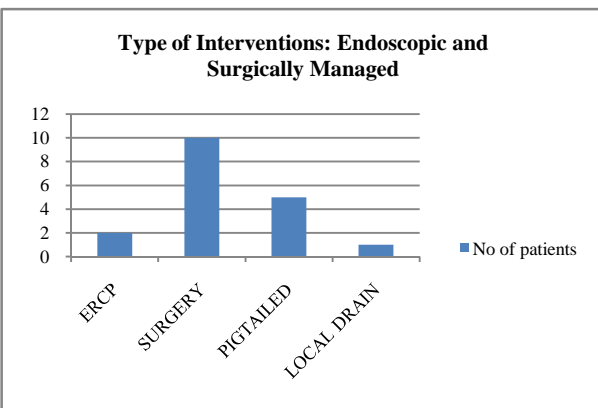**Fig 6** Distribution of type of Interventions

Fig 7 Intervention

Table 1 Ranson's Score and Intervention

		Conservative	Intervention	Total
Ranson Score				
	0-2	30	15	45
	>2	02	03	05
Total		32	18	50

P=0.23

Table 1 Distribution of SIRS in Acute Pancreatitis. (n=50)

	Alcoholic	Gall-stones	Idiopathic	Total
SIRS-				
YES	27	8	5	40
NO	7	3	0	10
TOTAL	34	11	5	50

Table 2 Ranson and Outcome Crosstabulation

		Outcome		Total
		Survived	Death	
Ranson				
	0-2	41	4	45
	>2	5	0	5
Total		46	4	50

P=0.48

Table 2 Laboratory parameters

Biochemical Tests	Frequency Of patients (out of 50)	Percentage of patients
1] ALP >120	11	22
2] LDH >350	36	72
3]SGOT >250	6	12
4] LIPASE 2X NORMAL	48	96
5] BUN RISE > 5 mg%	14	28

At admission, 8% had a Ranson's score of 0, 56% had a score of 1, 34% a score of 2, 2% had a Ranson's score of 3 or above. After 48 hrs, 4% had a score of 0, 34% had a score of 1, 52% had a score of 2, 10% had Ranson score of 3 [Figure 8].
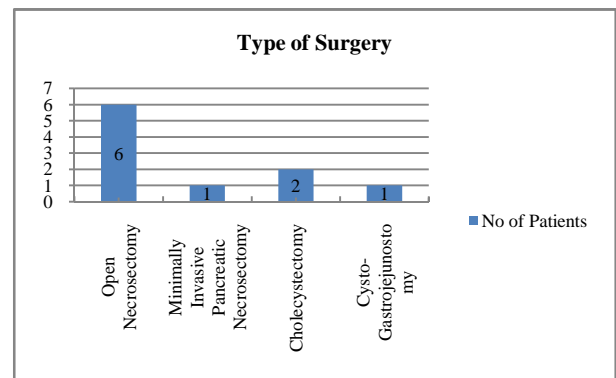

Fig 8 Distribution of Type of surgery

Nineteen patients had a Modified Balthazar's score of greater than 6 out of fifty patients [Table 3].

Table 3 CT Severity Index

CTSI SCORE	FREQUENCY	PERCENTAGE
0-5	31	62
>6	19	38
TOTAL	50	100

Twenty seven patients had pancreatic necrosis on imaging with 12 (24%) patients having a necrosis involving 30-50% of the gland and 10 (20%) patients showing an involvement of greater than 50% of the gland by necrosis [Figure 9 & 10]. There were several local [Figure 9] and miscellaneous complications which have been depicted in Table 5.

Table 4 CTSI and Intervention

		conservative	Intervention	Total
CTS				
	0-5	23	08	31
	6-10	09	10	19
Total		32	18	50

P=0.055

Eighteen (36%) patients required intervention. [Figure 11] Five patients needed percutaneous intervention in the form of pigtails to drain infected fluid collections and one patient had

to be local explored in order to place a drain into one such collection as the pigtail was not working effectively.

Table 5 CTSI and Outcome Crosstabulation

		Outcome		Total
		Discharged	Death	
CTSI				
	0-5	30	1	31
	6-10	16	3	19
Total		46	4	50

P=0.11

[Figure 12] Two patients needed ERCP and CBD clearance followed by stent placement. Although a few more patients needed ERCP it was deterred as they had presented beyond 48 hours of onset of pain. These patients had an ERCP performed at a later admission and hence have not been included here. Among those who required surgical intervention six patients had an open necrosectomy and one patient had necrosectomy perfomed by minimally invasive technique. Another patient needed an open cystogastrostomy for an infected pseudocyst. [Figure 13] Two patients were subjected to a cholecystectomy in the index admission as they had mild edematous pancreatitis [Figure 13].

There was no association between Ranson's score and the need for intervention. (P=0.23) [Table 6].

Table 6 local complications

	Frequency	Percentage
Peri-pancreatic necrosis	22	44
Pleural effusion	16	32
Fluid collection	28	56
Extraluminal gas/air	4	8
Pancreatic necrosis	27	54
Ascites	17	34

Similarly there was no statistically significant association between the CT Severity and the need for intervention. (P=0.055) [Table 7].

Table 7 Miscellaneous Complications

	Frequency	Percentage
Gastro-oesophageal varices	1	2
Extra hepatic biliary radical dilatation	3	6
Sup. Mesentric vein thrombosis	5	10
Portal vein thrombosis	4	8
Splenic vein thrombosis	5	10
Pseudo aneurysm	1	2
Peri organ inflammation	4	8

Ranson's score was unable to predict mortality significantly (P=0.48) [Table 8].

Table 8 Ranson and Outcome Crosstabulation

		Outcome		Total
		Survived	Death	
Ranson				
	0-2	41	4	45
	>2	5	0	5
Total		46	4	50

P=0.48

Neither was CTSI's ability to predict mortality (P=0.11) [Table 9]. The mortality rate was not significantly associated with the need for intervention. (P=0.830).

Table 9 Intervention and Outcome

	Outcome		Total
Management	Survived	Death	
Conservative	31	1	32
Intervention	15	3	18
Total	46	4	50

P=0.830

DISCUSSION

Of the 50 patients studied acute pancreatitis was more common in men versus women with an incidence of 78% [Figure.1]. The most affected people were between 21 to 50 years of age, the productive age group. The highest incidence was in the 31-40 and 41-50 age group. [Figure. 2] In a prospective study by Baig SJ on etiology, severity and outcome of acute pancreatitis in Eastern India the mean age was 30 years among 45 patients.[1] The findings in our study were close to their findings. Mean age of the patients in our study was 40.5 years.

The cause of acute pancreatitis was found to be either alcohol (34 patients) or gall stones (11 patients). While all who suffered from alcoholic pancreatitis were male, women formed the larger part of those who had gall stone induced pancreatitis (8). The data seems to be biased keeping in mind the Indian community of seldom alcoholic females. As also gall stone disease is more prevalent in women in most countries.[2] There was no cause found for the pancreatitis despite detailed workup in 5 patients of which 4 were women. We labeled them idiopathic. [Figure. 3]

The most common cause of acute idiopathic pancreatitis was found to be occult microlithiasis (up to 80% of patients), Sphinctor of Oddi dysfunction (30%), followed by papillary stenosis, pancreas divisum, pancreatic duct strictures and tumors.[3] An endoscopic ultrasound however did not diagnose any sludge or microlithiasis in the bile duct or gall bladder.

Forty patients had a documented systemic inflammatory response syndrome (SIRS) with alcoholic pancreatitis being the most common subgroup among them (27 Patients). Systemic inflammatory response can be found in the absence of necrosis initially. A severe inflammatory response can however lead to multiple organ failure. Patients with organ failure were found later on to have pancreatitis necrosis on imaging. [4] About 70 to 80% of patients had a temperature (34 patients), pulse (45 patients), respiration (44 patients) and WBC counts (39 Patients) fitting into the definition of SIRS. But we did not depend solely on the manifestation of SIRS to guide our management decision. Ranson's score was selected among the various Severity Scores at admission to predict which patients may proceed to a much severe form of pancreatitis. Figure. 4 depicts patients with various Ranson scores on admission and after 48 hours. As can be seen patients with scores below 2 showed a decreasing trend in 48 hours. Incidence of patients with a score of 2 and above showed an increasing trend after 48 hours. However none of this subset of patients had a score of 9 or above.

A study by Cho *et al*, found various scoring systems like Ranson, BISAP, CTSI, APACHE-II and CRP24 show similar predictive accuracy of severity. We chose Ranson and CTSI in our study in addition to SIRS to predict severity. [5] These two were easy to adapt into our protocol due to ease of implementation and availability. There was no significant

association between Ranson's score and the need for intervention. (P=0.23). [Table 1] Ranson's score also had no statistical significance in predicting mortality (P=0.48) [Table. 2]. A Ranson's criteria of 2 predicts zero mortality. If 3-4 criteria are positive the mortality is 15%, 5-6 indicates the possibility of 50% mortality and a score of >6, is likely to lead to 100% mortality. Perhaps the small sample size of our pilot study was a limitation.

In our study, patients were divided as per CTSI score into two sub groups. 62 % patients had score 0-5 and 38% patients had score > or equal to 6. [Table. 3] None of our patients suffered from organ failure however. The CTSI score however came very close to having a statistically significant association with intervention but the final value was not significant. (P=0.055) [Table. 4] There was no clinical significance between CTSI and mortality. (P=0.11) [Table. 5]. In 2010 a retrospective study by Xiao-Yan Li *et al* on prevalence and risk factors of organ failure in patients with severe acute pancreatitis out of 186 patients, 90 patients had no organ failure of which 57 patients (63.3%) belonged CTSI (0-6) and 33 patients (36.7%) belonged to CTSI (7-10). 17 (45.6%) and 22 (54.6%) patients with single organ failure belonging to CTSI (0-6) and CTSI (7-10) respectively. 12 (34.3%) and 23 (65.7%) patients with two organ failure of group CTSI (0-6) and CTSI (7-10) respectively . 7 (31.8%) and 15 (68.2%) patients with more than 2 organ failure of group CTSI (0-6) and CTSI (7-10) respectively. [6]

Robert *et al* had found that CT scan was insufficiently predictive of outcome [7] . A study by Vriens *et al* found CT to be an excellent prognostic tool for predicting complications and mortality. [8] The patients in this study had been grouped into three groups according to CTSI, (0-3), (4-6) & (7-10). It found that patients with a score between 0-3 could be easily observed outside the ICU. Our aim was quite the opposite - to find those patients who undoubtedly were in need of ICU care. In an over populated poverty ridden country like Indian, infrastructure falls far short of the demand. Intensive care units beds are always a far cry. Hence we are forced to triage every patient on admission to see who is in absolute need of intensive care and those in which general ward would suffice . Several studies either prove or disprove the importance of CT in predicting mortality of acute pancreatitis. Despite widespread research, no clinical or radiological or laboratory parameter has been persistently reliable in predicting mortality. On the contrary a combination of these variables improve the overall ability to predict severity.

A study in 2001 found there was very little reason to get an early CT especially in patients with Ranson's score less than 2 which is the reason for our protocol allowing a CT on or after day 5. However the same study also suggested a late CT, need not be performed routinely. That it should be done only the event of clinical or biological deterioration of the patient. [9] The findings in our study reflect the same message. About 44% of our patients had peri-pancreatic fluid collections, 32% had pleural effusions, 56% had pancreatic fluid collections and 8% had extra luminal gas on CT. 54% had pancreatic necrosis and 34% had pancreatic ascites. [Table 6]

In a retrospective study by Ai-Jun Zhu *et al*, 74 patients, 47 patients (63.5 %) showed systemic complications, 20 patients (27%) multiple organ complications, whereas 27 patients (36.5 %) with complications of a single organ system.

Pulmonary complications were the most common organ complications among single organ complications. They found no significant differences in age, gender and gallstone pancreatitis among patients with or without organ complications.[10] The most common complication in our study was pancreatic fluid collections. The less common complications were gastroesophageal varices (1), extrahepatic biliary radical dilatation (3), SMV thrombosis (5), PV thrombosis (4), splenic vein thrombosis (5), pseudoaneurysm (1) and peri-organ inflammation (4). [Table 6] These included the colon and the mesocolon. 2% patient had hemorrhage/ rupture of pseudo cyst. These less common complications were all detected on CT and were by themselves asymptomatic. 22% (11) patients developed necrosis had necrosis in more than 50% of the gland. 24% had a necrosis between 30-50% of the parenchyma and 8% (4) patients had necrosis involving less than 30% of the parenchyma [Figure. 5].

A total of 18 out of 50 patients required interventions. 4% of the patients with pancreatitis required ERCP, while 32% patients required surgical or radiological interventions like ERCP: 4%, Surgery 20%, Pigtail10%, local insertion of large bore drain 2%, Surgery was performed in the form of open necrostomy: 12%, cholecystectomy: 4%, cystogastrostomy in 2% and MIPN in 2% [Figure 6,7&8]. The death rate in patients with intervention done was found to be 3/18 i.e. 16.67%. While the death rate in conservatively managed patients was found to be 1/32 i.e.3.125%. However the difference in the mortality rate was not found to be statistically significant.

We did not attempt a more detailed analysis of the data collected from this pilot study as the small sample size had already proved there were no statistically significant findings with the parameters we had attempted an analysis with. The study design however proved itself to be feasible to be applied to a larger study of a hundred patients, which was the main reason behind conducting this pilot study and we hope to work on the larger data from the final study soon.

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