IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 18, Issue 3 Ser. 16 (March. 2019), PP 51-58
www.iosrjournals.org

A Clinicopathological Study of Necrotizing Pancreatitis with Special Emphasis on Need for Surgery and Its Outcome

Debasis Ray[1], Vishal Jalan[2], Sudeb Saha[3]
[1] *Associate Professor & MS in the Department Of Surgery, Nil Ratan Sirkar Medical College, Kolkata, West Bengal India*
[2] *MS 3nd Year Post Graduate student, in the Department Of Surgery, Nil Ratan Sirkar Medical College, Kolkata, West Bengal India*
[3] *Professor & MS in the Department Of Surgery, Nil Ratan Sirkar Medical College, Kolkata, West Bengal India*
Corresponding Author: Debasis Ray

Abstract: *Necrotizing pancreatitis is one of the important causes of mortality in acute pancreatitis especially when it is infected. Intervention is very rarely indicated in patients with sterile necrosis but may be required in those who continue to deteriorate despite maximal supportive care. In contrast, patients with infected pancreatic or peri-pancreatic necrosis almost always require intervention. Although infected pancreatic necrosis has been considered an absolute indication for surgical intervention, cases successfully managed non-surgically have been reported. This study assessed the course of necrotizing pancreatitis with and without surgical intervention.*

This observational study was conducted in NilRatan Sircar medical college & hospital, on patients admitted with Acute Pancreatitis and latter diagnosed to have Acute Necrotizing Pancreatitis (on the basis of Contrast Enhanced CT Scan of Whole Abdomen) during January 2015 to September 2016.Thirty patients who fulfilled the inclusion criteria were enrolled for the study .There was a male preponderance. 50% of cases occurred in the age group of 30 to 49 years. Gall stone was the most common etiological agent followed by alcoholism and also gall stone was most common cause of infected necrotizing pancreatitis being present in 67% cases. Esch.coli was the most common organism found in infected necrotizing pancreatitis. CRP >= 150mg/L was 82% sensitive and 56% specific in diagnosing severe pancreatitis with CTSI > 6 73% of patients with acute necrotizing pancreatitis had less than 50% necrosis .64% of the patients (n=22) were managed conservatively. Rest 8 patients with >50 % necrosis had to undergo necrosectomy. One patient out of the 22 patients managed conservatively and 3 patients out of the 8 managed surgically died of various complications.

Key words*: Pancreatitis, Necrotising pancreatitis, C Reactive Protein, Necrosectomy,*

Date of Submission: 20-03-2019 Date of acceptance: 06-04-2019

I. Introduction

Necrotizing pancreatitis is one of the important causes of mortality in acute pancreatitis especially when it is infected. Intervention is very rarely indicated in patients with sterile necrosis but may be required in those who continue to deteriorate despite maximal supportive care. In contrast, patients with infected pancreatic or peri-pancreatic necrosis almost always require intervention. Although infected pancreatic necrosis has been considered an absolute indication for surgical intervention, cases successfully managed non-surgically have been reported.[1,2] This study assessed the course of necrotizing pancreatitis with and without surgical intervention.

II. Aims And Objectives

To study the course of Necrotizing Pancreatitis with history, clinical examination, routine &specific pathological and biochemical tests & imaging studies

To access need of surgical intervention and its outcome and to compare the results of the presentstudy with other published articles on necrotizing pancreatitis

III. Methods

This observational study was conducted in NilRatan Sircar Medical College & Hospital, in patients admitted with Acute Pancreatitis and latter diagnosed to have Acute Necrotizing Pancreatitis (on the basis of Contrast Enhanced CT Scan of Whole Abdomen) during January 2015 to September 2016.

The diagnosis of acute pancreatitis was based on the modified Atlanta classification which requires two of the following three features: (1) *abdominal pain* consistent with acute pancreatitis (acute onset of a persistent, severe, epigastric pain often radiating to the back); (2) serum *lipase activity (or amylase activity) at least three*

times greater than the upper limit of normal; and (3) characteristic findings of acute pancreatitis on contrast-enhanced computed tomography (CECT) and less commonly magnetic resonance imaging (MRI) or transabdominal ultrasonography.
Written consent were obtained from the patients
Children less than 12 years were exclude from the study

Patients with acute necrotizing pancreatitis were enrolled for the study after fulfilling the inclusion criteria and after having obtained written consent. Patients were assessed at admission by history, clinical examination, necessary investigations (like serum amylase, serum lipase, complete blood count, CRP, ultrasonography whole abdomen etc.). Initially the patients were managed with intravenous fluid resuscitation, analgesic and supportive care. Antibiotics were not used prophylactically. Patients were reviewed periodically regarding pain, tolerance to enteral feeding, vital parameters and blood investigations. When the above mentioned parameters were non resolving, or there is presence of persistent disease or progressive disease, the patients were subjected to CECT Whole Abdomen to ascertain the presence and extent of pancreatic necrosis. Further course of management was decided on the basis of CECT findings.

IV. Results

Between January 2015 to September 2016, 30 patients were diagnosed with Acute Necrotizing Pancreatitis . The male female ratio was 1.7:1 (chart 1). Around 50% of cases occurred in the age group 30 to 49 years (chart 2). Gall stone was found to be most common etiological agent being present in 43% of cases whereas alcoholism was responsible for another 37 % of cases and in 6 cases no cause could be determined (Chart 3).

In this study we found that there is a significant relationship (p-value <0.05) between CRP and CTSI (CT SEVERITY INDEX). When the CRP is ≥ 150mg/L there is high probability of having severe pancreatitis (Table 1). Out of the 13 cases of gall stone pancreatitis, in 4 cases necrosum was found to be infected (3 cases were infected with Esch.Coli, and 1 case with Klebsiella Sp). Out of the 11 cases of alcoholic pancreatitis, in 2 cases necrosum was found to be infected (both with E.Coli) and in the remaining 6 cases (of unknown etiology) were found to be sterile (chart 4). In this study, only 27% (8 out of 30) cases have necrosis > 50%. In this study we found that in the patients with <50% necrosis, the necrosum was sterile. On the other hand, 6 out of 8 patients with >50% necrosis got infected in the necrosum. In our study, majority (73%, n=22) of the cases were managed conservatively. Out of the 8 patients, managed surgically, 3 patients died and of the 22 patients managed conservatively, one died.

We also observed that patients with CTSI (CT SEVERITY INDEX) ≤ 7 required conservative management and patients with CTSI ≥7 required surgical management with open necrosectomy.

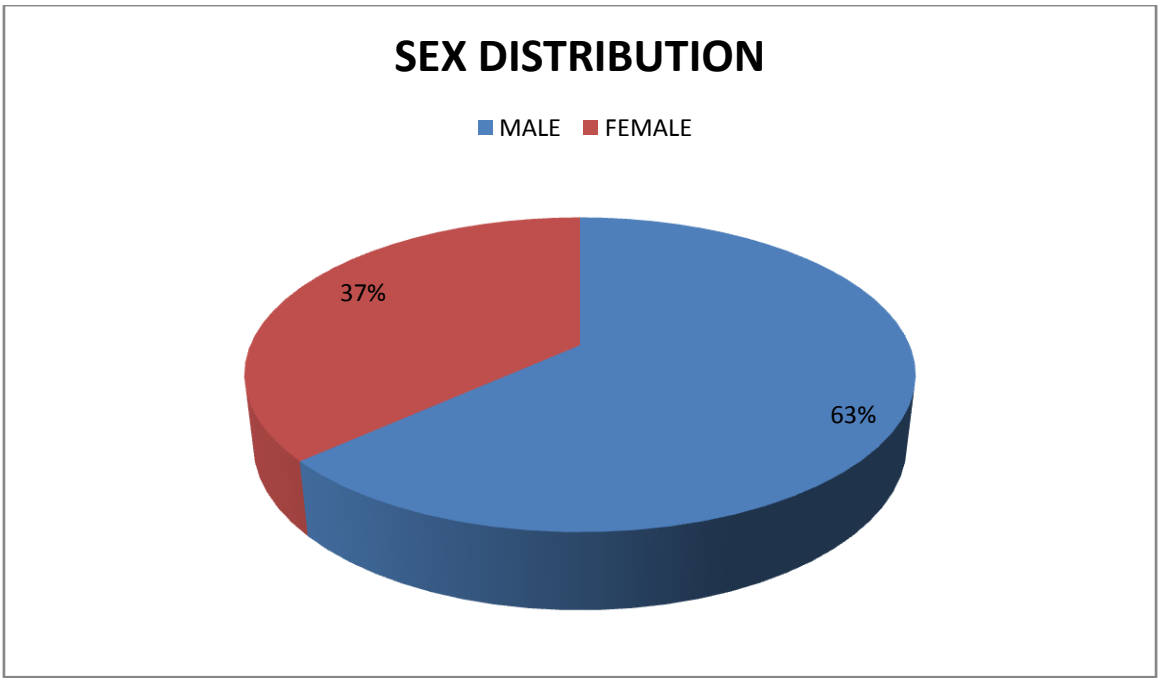

Chart 1 depicting male female ratio (19 are male that is 63% and 11 are female that is 37%.).

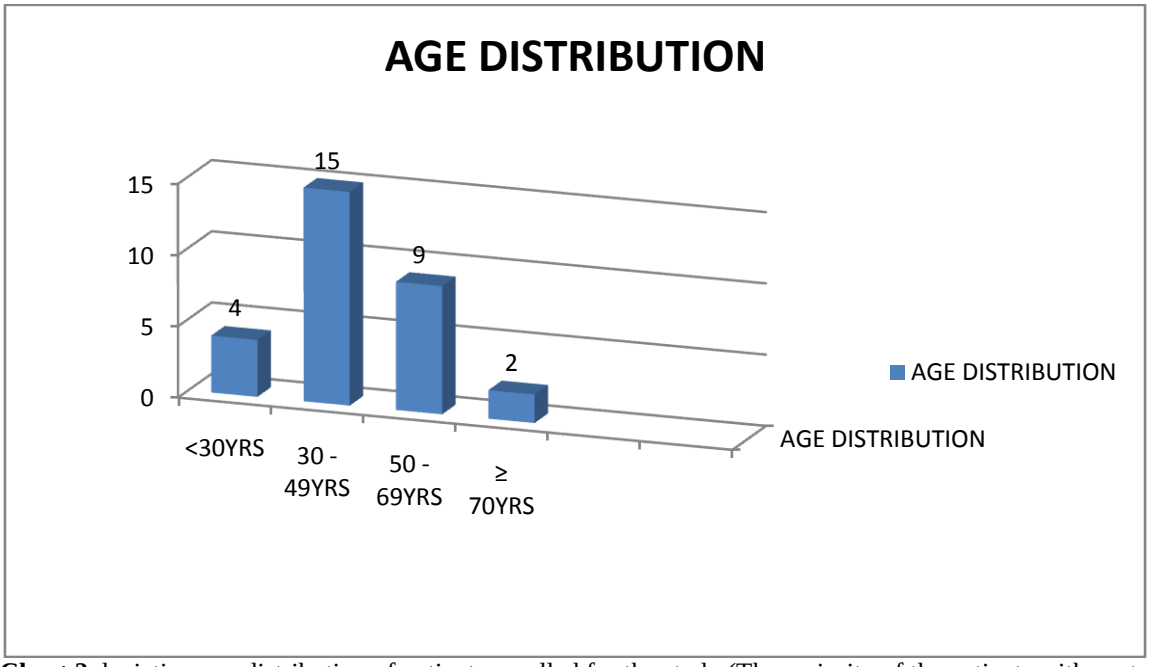

Chart 2 depicting age distribution of patients enrolled for the study (The majority of the patients with acute necrotizing pancreatitis are in 30 – 49 years of age group that is 50%. 30% are in the age group 50 – 69 years, 13% in <30 years and rest 7% in ≥ 70 years).

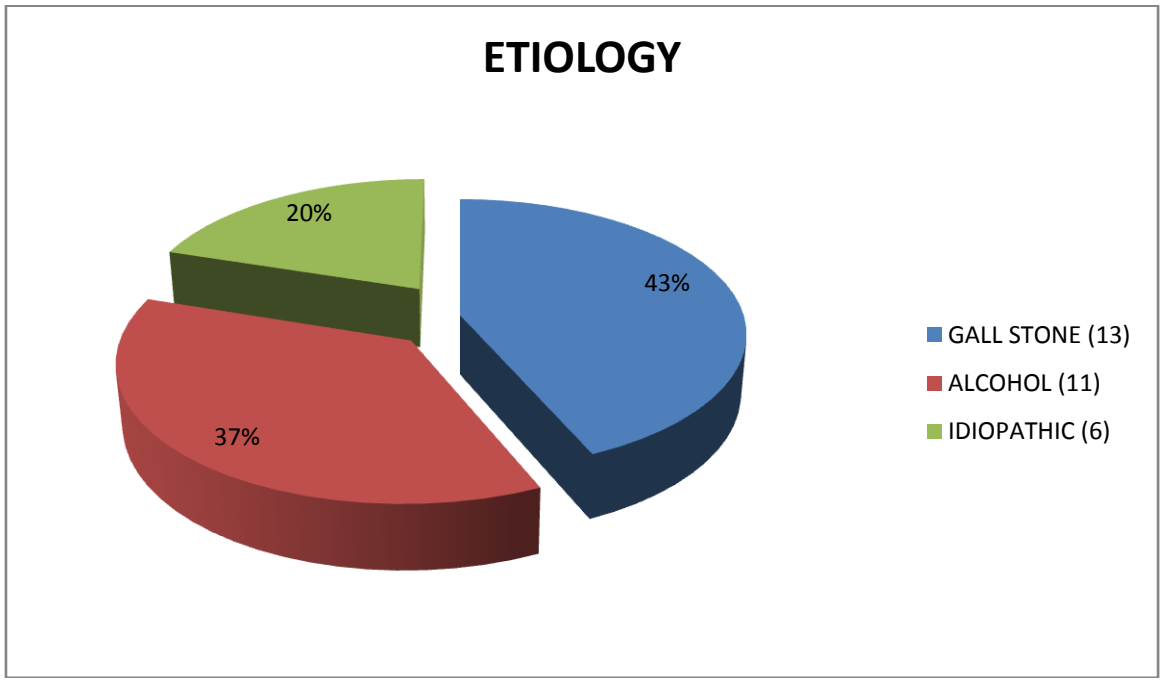

Chart 3 depicting the etiology of acute necrotizing pancreatitis

Table 1

Patients with CTSI	Pts with CRP <150mg/l	Pts with CRP ≥ 150mg/l
< 6	5	4
≥ 6	4	17

Chi-square = 4.00, df = 1, p-value = 0.046

Table 1 depicts relationship (p-value <0.05) between CRP and CTSI.

Chart 4

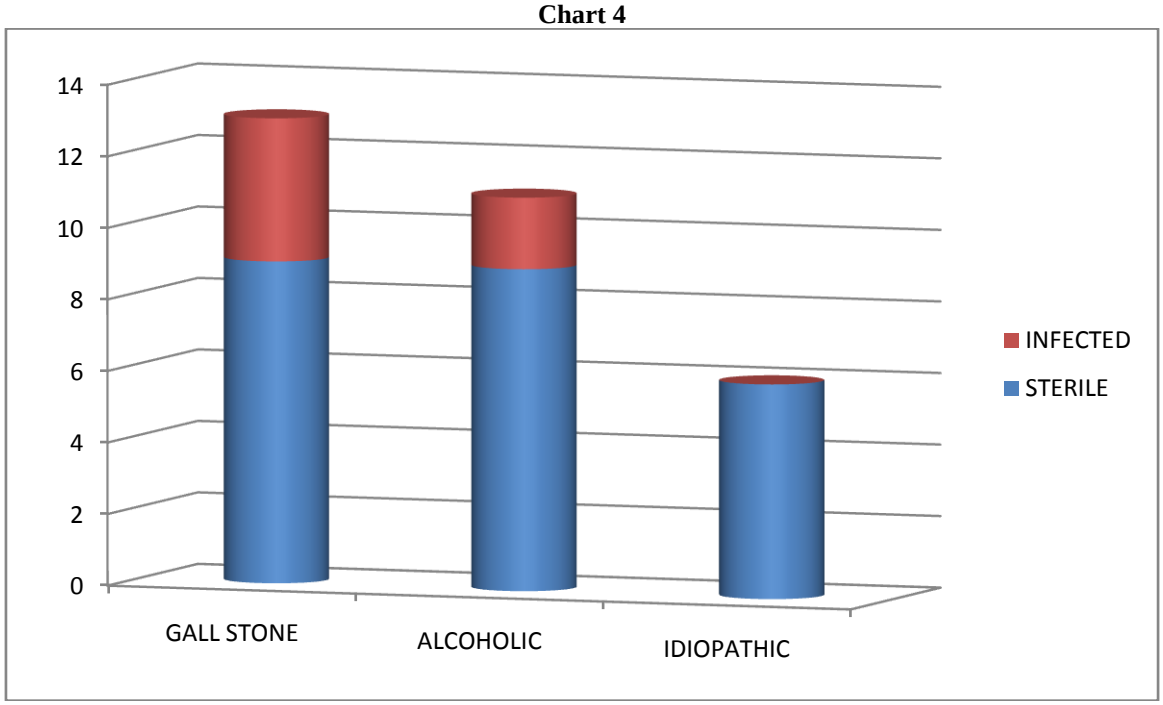

Chart 4 This bar diagram shows that out of 30 cases of acute necrotizing pancreatitis 13 cases are due to gall stone disease, 11 cases due to chronic alcohol consumption and in 6 cases not cause found out. Out of 13 cases of gall stone pancreatitis, in 4 cases necrosum was found to be infected (3 cases was infected with E.Coli, and 1 case with Klebsiela Sp). Out of 11 cases of alcoholic pancreatitis, in 2 cases necrosum was found to be infected (both with E.Coli). and all the cases the 6 cases (in which no cause was found out) was found to be sterile

V. Discussion

Acute pancreatitis is a disease with substantial burden on the health care system. Recent data indicate a rise in absolute number as well as rate of emergency room visits, hospital admissions and direct health care cost for acute pancreatitis. According to the inflammatory changes in pancreatic parenchyma, acute pancreatitis may be classified as interstitial oedematous or necrotizing. Necrotizing pancreatitis is the presence of one or more diffuse or focal area of non-viable pancreatic parenchyma[3, 4, 5].

Necrotizing pancreatitis is one of the important causes of mortality in acute pancreatitis especially when it is infected. Intervention is very rarely indicated in patients with sterile necrosis but may be required in those who continue to deteriorate despite maximal supportive care. In contrast, patients with extensive infected pancreatic or peri-pancreatic necrosis almost always require intervention, as this complication is the most significant determinant of outcome. Although infected pancreatic necrosis has been considered an absolute indication for surgical intervention, cases successfully managed conservatively have been reported [6,7, 8].

This observational study was conducted in a tertiary care medical college and hospital, on patients admitted with acute pancreatitis and latter diagnosed to be acute necrotizing pancreatitis (on the basis of contrast enhanced CT scan of whole abdomen) during a period of 18 months. A total of 30 patients were enrolled for the study after conforming to the inclusion criteria and giving written consent for being included in the same.

Of the 30 patients, 19 patients were male and 11 were female, indicating a clear male prevalence. With the male : female ratio 1.7:1. This is in conformance with other similar studies as depicted below.

STUDY	**MALE (M)**	**FEMALE (F)**	**M:F RATIO**
Buchler MW *et al* [9]	125	79	1.6:1
Jiang W *et al* [10]	79	40	1.98:1
Doctor N *et al* [11]	49	12	4.1:1

Alvi AR *et al* [12]	31	16	1.9:1
Birgisson H *et al* [13]	27	23	1.2:1
Present study	19	11	1.7:1

Of the 30 patients, 15 were in the age group of 30-49 years (50%), with the mean age being 45.9 years ±15.7. This finding is in conformance with the majority of the studies. Buchler MW *et al*, Jiang W *et al*, Doctor N *et al*, PANTER trial reported the mean age of patients with necrotising pancreatitis as 55.1,45.1, 43 and 57 years respectively [9.10,11,14] .

In the present study, we found that gallstones was the most common etiological factor present in 43% of patients and alcohol come second being present in 37% of patients. This is comparable with the majority of other studies except few (Nordback I *et al*) in which authors reported alcohol as the most common etiological factor. The comparative figures are outlined below.

STUDY	**GALLSTONE**	**ALCOHOL**	**OTHER CAUSES**
Birgisson H *et al*[11]	42%	32%	24%
Doctor N *et al*[13]	41%	23%	36%
Alvi AR *et al*[10]	46%	9%	45%
Nordback I *et al*[15]	16%	70%	14%
Present study	43%	37%	20%

We observed that majority of patients with CRP ≥ 150mg/L were latter diagnosed to have severe pancreatitis on the basis of biochemical (renal function test, pulmonary function test etc) and imaging modalities (CECT whole abdomen)

As with other studies, this study also reflected the comparable result so far as the sensitivity of CRP as a marker of severity is concerned (i.e. 82%) but we found the specificity (CRP ≥ 150mg/L) to be only 56% . Other similar studies have found specificity from 74% to 86%. But as the p-value obtained in our study is 0.46, which proves there is significant relationship between rise of CRP ≥ 150mg/L and severe pancreatitis. The different studies which evaluated CRP values as a marker of severity of pancreatitis is depicted below.

STUDY	**CRP VALUE**	**SENSITIVITY**	**SPECIFICITY**
Buchler MW *et al* [9]	>100mg/L	100%	86%
Alfonso V *et al*[16]	>200mg/L	88%	75%
Gurleyik G *et al*[17]	>150mg/L	85%	74%
Present study	≥150mg/L	82%	56%

In this study, we have found that gall stone was the most common cause of infected necrotizing pancreatitis being present in 67% (4 out of 6 patients) and alcohol was the second common cause being present in 33% cases. This was comparable with the study by Buchler MW *et al* as depicted below [9].

ETIOLOGY	**STERILE**	**INFECTED**
GALL STONE	39%	55%
ALCOHOL	40%	31%
OTHER	21%	14%

Present study

ETIOLOGY	**STERILE**	**INFECTED**
GALL STONE	69%	31%
ALCOHOL	82%	18%
OTHER	100%	0%

In our study, only 8 out of 30 patients had >50% whereas 22 patients have <50% necrosis in the pancreas. This is low as compared to other similar studies. This might be due to low number of cases recruited in this study. The comparative figures are shown below

STUDY	<50% NECROSIS	>50% NECROSIS
PANTER trial [9]	57%	43%
.Buchler MW *et al* [14]	63%	37%
Nordback I *et al*[15]	61%	39%
Present study	73%	27%

In our study, 75% of patients with >50% necrosis became infected which is comparable with other studies. But in this study cases with < 50% necrosis did not develop infection of the necrosum which is not seen in other similar studies. Again this might be due to the limited number of cases in this study. The findings by Buchler MW *et al* [9] and the present study is shown below.

% necrosis	**sterile**	**Infected**
<50%	**89% (48 out of 54)**	**11% (6 out of 54)**
>50%	**28% (9 out of 32)**	**72% (23 out of 32)**

Present study

% necrosis	**sterile**	**Infected**
<50%	**100% (22 out of 22)**	**0% (0 out of 22)**
>50%	**25% (2 out of 8)**	**75% (6 out of 8)**

In this study, 22 out of 30 patients were managed conservatively and 8 out of 30 patients were managed surgically (i.e. majority of patients were managed conservatively). This is comparable with majority of other studies

STUDY	CONSERVATIVE	SURGICAL
Buchler MW *et al* [9]	63%	37%
Alvi AR *et al* [10]	47%	53%
This study	64%	36%

In this present study, 8 out of 30 patients underwent open necrosectomy (based on patient's condition and CT guided Fine Needle Aspiration report). Of the 8 patients, who were treated surgically three patients died. One of them died in the immediate post operative period due to sudden cardiac arrest. Rest of them died due to sepsis with multiorgan failure one at 2nd post operative day and the other at 5th post operative day

STUDY	MORTALITY RATE IN SURGICAL TREATMENT
Bradley EL 3rd	15%
Buchler MW *et al* [9]	21%
Alvi AR *et al*[10]	38.9%
Santvoort HCV *et al* [14]	15.6%
Doctor N *et al*[13]	10%
Present study	37.5%

This table shows that in majority of studies death rate was between 10 to 21%. But in this study death rate was much higher (37.5%).

In our study, 5 out of 8 patients (managed with open necrosectomy) survived post operatively; of these 3 patients developed pancreatic fistula (60%). The diagnosis of pancreatic fistula was based on amylase estimation of the drain fluid, which ranged from 9000 to 30,000 U/mL. The drainage tube was maintained in situ and the patient was managed on conservatively till the drain bag was dry for 3 consecutive days. One out of 5 patients who survived post-operatively developed incisional hernia which was managed with open mesh repair. Rest one patient developed wound infection on 5th post-operative day which was managed with skin suture removal and drainage of pus, regular dressing with normal saline (0.9%), anti-microbial agents according to culture and sensitivity report of pus. Secondary suturing was done on 29th post-operative day. In PANTER trial, the rate of development of pancreatic fistula and incisional hernia was 44.7% and 45.8% respectively in operated cases[14.] In the study by Buchler M W *et al* pancreatic fistula developed in only 29% of post-operative cases[9]. Doctor N *et al* found pancreatic fistula rate of 50.8% and wound infection rate of 29.5% in post-operative patients in his study[13]. In this study, we have not found any of these patients who underwent open necrosectomy develop enteric fistula, intestinal obstruction, pseudocyst formation, pelvic abcess, DIC etc, as seen in other studies.

In our study, 22 out of 30 patients were managed conservatively of them only one patient died (4.6%). This is comparable with other studies. As the p-value is 0.019 suggesting that there is a significant relationship between conservative treatment and chance of survival. i.e. patients with acute necrotizing pancreatitis are less likely to die when compared to the patients managed with open-necrosectomy (37.5%, 3 out of 8).

STUDY	MORTALITY RATE IN CONSERVATIVE TREATMENT GROUP	MORTALITY RATE IN SURGICAL TREATMENT GROUP
Buchler MW *et al* [9]	5% (3 out of 58)	21% (6 out of 28)

Alvi AR *et al*[10]	6.9% (2 out of 29)	19.7% (4 out of 18)
Present study	4.6% (1 out of 22)	37.5% (3 out of 8)

In the present study, we have found that out of 22 patients with **CTSI ≤ 7** ,21 patients were managed conservatively and one patient was managed surgically. And out of 8 patients with **CTSI > 7** ,one patient was managed conservatively and 7 were managed surgically. This suggest that as the CTSI increases it becomes difficult to manage the patients conservatively. We have also found in this study that patients with >50% necrosis are more prone to develop infected necrotizing pancreatitis which itself is an indication for open necrosectomy.

In our study, mean duration of hospital stay of the patients managed conservatively was 11.14days ± 21.9days (mean ± sd) and those managed with open-necrosectomy was 50.5days ± 32.7 (mean ± sd), which was > 4 times when compared to conservative treatment group. In PANTER trial median of duration of stay (in hospital) of the patients in surgical group was 60 days (range 1-247days)[14]. Cinquepalmi L *et al* found in his study that mean duration of stay in hospital of patients managed with surgery due to infected pancreatic necrosis was 71days ± 38[19]. Doctor N *et al* found in their study that the median duration of hospital stay following surgery was 23 days (range 11-88 days) [13].

VI. Conclusion

There was a male predominance in the incidence of acute necrotizing pancreatitis in a 1.7:1 ratio.
Most cases occurred in the age group of 30-49years.
Gallstones was the most common etiological factor present in 43% of the patients, followed by alcoholism (37%).
There was a significant relationship between CRP and severity of pancreatitis (measured with CT severity index). CRP ≥ 150mg/L was 82% sensitive and 56% specific in diagnosing severe pancreatitis with CTSI > 6, having p-value = 0.46.
Gallstones was the most common cause of infected necrotizing pancreatitis being present in 57% pf patients and alcohol was the second common being present in 33% of patients.
Escherichia coli was the most common organism found in infected necrotizing pancreatitis.
Majority of patients with acute necrotizing pancreatitis had <50% necrosis (73%).
Patients with <50% necrosis was less prone to develop infected necrotizing pancreatitis. As the percentage of necrosis increases more than 50% chances of getting infected also increases.
Most patients improved on conservative management (22 out 30 patients were managed conservatively of which 21 patients survived.).
As the CTSI increased numbers of patients managed conservatively were decreased. All the patients with CTSI > 8 were managed with open necrosectomy.
Patients managed conservatively were hospitalised for lesser duration (11.14 days ± 21.9) when compared to patients managed with open necrosectomy (50.5 days ± 32.7). Due to which the cost of treatment of patients managed conservatively was much lesser when compared with patients managed surgically (open necrosectomy).
Pancreatic fistula was the most common complication being present in 60% of patients managed with open necrosectomy. Other complications were incisional hernia and wound infection.
Death rate among the patients managed conservatively was much lower (4.5%. 1 out of 22 patients) when compared to death rate among patients managed with open necrosectomy (37.5%, 3 out of 8 patients).

References

[1]. Howard, J. M. *History of the pancreas. The pancreas club*, 2014. Web.
[2]. Trede M, Carter D C, and Longmire W P Jr. "history of pancreatic surgery." *Surgery of the pancreas*. USA: Churchill Livingstone, 1993. p 1-15.
[3]. Townsend CM, Beauchamp RD, Evers BM, Mattox KL, Exocrine Pancreas. *Sabiston textbook of surgery*. 20th ed, Philadelphia: Elsevier, 2016: p 1523-24.
[4]. Brunicardi FC, Andersen DK, Billiar TR, Dunn DL, Hunter JG, Matthews JB, Pollock RE. Pancreas. *Schwartz's Principles Of Surgery*. 10th ed, US: Mc Graw Hil, 2015: p 1348-49.
[5]. Befer HG, Rau BM: Severe acute pancreatitis: Clinical course and management. *World J Gastroenterol* 13:5043-5051, 2007.
[6]. Banks PA, Freeman ML. Practice guidelines in acute pancreatitis. *Am J Gasteroenterol* 2006;101:2379-400.
[7]. UK Working party on Acute pancreatitis. UK guidelines for the management of acute pancreatitis. *Gut* 2005; 54: iii 1-9.
[8]. Uhl W, Warshaw A, Imrie C, et al. IAP Guidelines for the surgical management of acute pancreatitiis. Pancreatology 2002; 2: 565-73
[9]. Buchler MW,Gloor B., Muller CA, Friess H, Seiler CA, Uhl W. Acute necrotizing pancreatitis: treatment strategy according to the status of infection. *Ann Surg*. 2000;3:93-101.
[10]. Alvi AR, Sheikh GM, Kazim SF. Delayed surgical therapy reduces mortality in patients with acute necrotizing pancreatitis. J Pak Med Assoc. 2011 Oct;61(10):973-7.

[11]. Birgisson H[1], Möller PH, Birgisson S, Thoroddsen A, Asgeirsson KS, Sigurjónsson SV, Magnússon J . Acute pancreatitis: a prospective study of its incidence, aetiology, severity, and mortality in Iceland. Eur J Surg. 2002;168(5):278-82.
[12]. Chaw-Fung Jiang, Yu-Chien Shiau, Kam-Wing Ng, So-Wan Tan. Serum Interleukin-6, Tumor Necrosis Factor and C-reactive Protein in Early Prediction of Severity of Acute Pancreatitis. J Chin Med Assoc. ssoc 2004;67:442-446
[13]. Doctor N, Philip S, Gandhi V, Hussain M, Barreto SG. Analysis of the delayed approach to the management of infected pancreatic necrosis. *World J Gastroenterol*. 2011;17(3):366-71.
[14]. Van Santvoort HC, Besselink MG, Bakker OJ, et al. A step-up approach or open necrosectomy for necrotizing pancreatitis (PANTER trial). *N ENGL J Med* 2010;362:1491-502.
[15]. Nordback I, Lauslahti K. Clinical pathology of acute necrotising pancreatitis. *J Clin Pathol*. 1986;39(1):68-74.
[16]. Alfonso V, Gómez F, López A, Moreno-Osset E, del Valle R, Antón MD, Blanes F, Ripollés T, Ortiz I . Value of C-reactive protein level in the detection of necrosis in acute pancreatitis . Gastroenterol Hepatol. 2003 May;26(5):288-93.
[17]. Gürleyik G[1], Emir S, Kiliçoglu G, Arman A, Saglam A ,Computed tomography index, APACHE II score, and serum CRP concentration for predicting the severity of acute pancreatitis. JOP. 2005 Nov 10;6(6):562-7.
[18]. Bradley EL. Management of infected pancreatic necrosis by open drainage. *Ann Surg*. 1987; 206 (4):542-50.
[19]. Cinquepalmi L, Boni L, Dionigi G, Rovera F, Diurni M, Benevento A, Dionigi R . Long term results and quality of life of patients undergoing sequential surgical treatment for acute pancreatitis complicated by infected pancreatic necrosis. Surg Infect (Larchmt). 2006;7 Suppl 2:S113-6

Debasis Ray. "A Clinicopathological Study of Necrotizing Pancreatitis with Special Emphasis on Need for Surgery and Its Outcome." IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 18, no. 3, 2019, pp 51-58.