



## Study of Surgical Complications of Pancreatitis

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### Abstract

**Aims and Objectives:** (1) Study of patients of pancreatitis with respect to their complications requiring surgical intervention. (2) To study prognosis of patients after surgical treatment of complications of pancreatitis.

**Study Design:-** This was a descriptive study carried out in a tertiary care centre over a period of 18 months and included patients of acute and chronic pancreatitis with their surgical complications.

**Materials and Methods:-** The study was approved by the Institutional ethical committee and included patients of acute and chronic pancreatitis with their surgical complications. Patients were included in this study only after being diagnosed as a complication of pancreatitis needing surgical intervention. Informed consent was obtained after explaining all patients regarding disease outcome and possible complications related to surgical treatment. Patients having history of trauma, those who denied consent, those in whom regular follow up was not possible and those who didn't give consent were excluded from the study.

**Results:** The study of surgical complications of pancreatitis revealed that the peak incidence of their occurrence was in between age group of 30 to 39 years (29.54%) followed by in the age group of 40-49 years (15.90%). Predominantly males were affected with a male to female ratio being 1: 0.12. The most common etiology was found to be alcohol (68.18%) followed by idiopathic (15.90%) and malnutrition (11.36%). The most common presenting complaints were pain (90.90%) followed by weight loss (86.36%) and steatorrhea (43.18%). On clinical examination the most common physical finding was tachycardia (29.54%), icterus (20.45%) and raised temperature (18.18%). Blood investigations most common abnormalities found were anemia, leucocytosis, hyperbilirubinemia, and increased serum lipase levels. On X-ray Pleural effusion and abdominal calcifications was found in 13 (29.54) and 12 (27.27%) patients respectively. The most common surgical complication in studied cases were pseudocyst formation (36.36%), ductal dilatation with without ductal calculi (25%) and pancreaticopleural effusion (15.90%). Uncomplicated pseudocyst (31.81%), pancreatic calcification (27.27%), pancreatic ductal calculi (20.45%), atrophy of pancreas (20.45%) and CBD dilation (20.45%) were the most common imaging abnormalities seen in CT and MRCP. Obstructive jaundice was seen in 9 (20.45%) patients. The most common surgical procedure done in studied cases was intercostal drain insertion for pleural effusion which was done in 7 (15.90%) other common surgical procedures were laparoscopic cystogastrostomy (4.54%), and laparoscopic LPJ (9.09%). Laparoscopic surgeries were done in 16 (36.36%) cases while open surgeries were done in 28 (63.63%) patients. Immediate post-operative

complications included wound infection (9.09%), bleeding (4.54%) and anastomotic leak (4.54%). Common late post-operative complications were Deranged blood sugar levels (11.36%), intra-abdominal abscess (6.81%) and weight loss (6.81%). Amongst the patients operated for pancreatic pseudocyst only 1 patient presented with pseudocyst recurrence 6 months after initial surgery. Puestow procedure was most commonly associated with weight gain. All 6 (100%) patients had weight gain after this procedure while necrosectomy was least associated (20%) with weight gain. The most effective procedure in terms of pain relief was puestow procedure in which 6 (85.71%) out of 7 patient had pain relief. The overall mortality in the study was found to be 6.81%.

**Keywords:** Pancreatitis, Surgical complications, prognosis, disease outcome.

## Introduction

Pancreatitis is an inflammation of pancreas and its surrounding structures. Acute pancreatitis is an inflammation of glandular parenchyma leading to injury or destruction of acinar components<sup>[1]</sup>. The pathologic process could results in self limiting disease with no sequelae or in catastrophic auto digestion activity with systemic cytotoxic effects and life threatening complications in acute form<sup>[2]</sup>.

Chronic pancreatitis is syndrome involving progressive inflammatory changes in the pancreas that result in permanent structural damage, which leads to impairment of exocrine and endocrine function<sup>[3]</sup>.

In the past 15 years there has been a great lead in the knowledge of natural history of acute and chronic pancreatitis and at the same time major advances in imaging of pancreas. Thus it has become possible to classify the severity of the disease and to assess the evolution of pancreatitis in real time. This has enabled the objective assessment of various new approaches designed with the objective of significantly reducing the morbidity and mortality of this disease<sup>[4]</sup>.

During recent years the management of acute pancreatitis has changed. This has been due particularly in response to the general availability of computed tomography, improved intensive care facilities, knowledge about the central role of pancreatic infection and refinements in surgical and other interventional techniques to treat Surgical Complications of Pancreatitis<sup>[5]</sup>.

Diagnostic improvements in form of MRCP, ERCP, EUS have made diagnosis easy and many cases are being diagnosed early<sup>[6]</sup>. The

indications for surgical intervention are intractable pain, complications related to adjacent organs, pancreatic, pseudocysts, ductal pathology, and intractable internal pancreatic fistula<sup>[7]</sup>. Furthermore, the inability to exclude pancreatic cancer despite broad diagnostic work-up also requires surgery<sup>[8]</sup>. The ideal surgical approach should address all these problems – tailoring the various therapeutic options to meet the individual patient's needs<sup>[9]</sup>. The common complications which need surgical intervention are pseudocyst formation, obstructive jaundice, splenic vein thrombosis and portal hypertension and pancreatic abscess<sup>[10]</sup>.

## Materials and Methods

This was a descriptive study carried out in a tertiary care centre from January 2015 to July 2016 and included patients of acute and chronic pancreatitis with their surgical complications (complications of pancreatitis which require any type of surgical intervention) i.e. pseudocyst of pancreas, necrotizing pancreatitis, pancreatic abscess, pancreaticopleural fistula, chronic pancreatitis with pancreatic duct dilation with or without ductal calculi, chronic pancreatitis limited to pancreatic head, post pancreatitis splenic vein thrombosis with portal hypertension with gastric varices and chronic pancreatitis limited to pancreatic head.

Total 44 patients were included in this study. Patients were included in this study only after being diagnosed as a complication of pancreatitis needing surgical intervention. Informed consent was obtained after explaining all patients regar-

ding disease outcome and possible complications related to surgical treatment.

**Inclusion criteria:** All patients of acute and chronic pancreatitis with complications which needed surgical intervention.

**Exclusion Criteria:** (1) Patients who were not ready for regular follow up. (2) Patients who had not given consent for surgical intervention. (3) Requiring endoscopic management only or radiological intervention only. (4) Patients with pancreatic trauma.

Once the patients were diagnosed as a case of complication of pancreatitis needing surgical intervention, detailed history and clinical examination was carried out. Again basic investigations were advised if required for further definitive management of respective surgical complication of pancreatitis. These investigations included chest X-ray, X-ray abdomen, CT abdomen and pelvis with contrast, MRCP (Magnetic Resonance Cholangiopancreatography). All Blood investigation mentioned in this study were done when surgery of respective patient was planned. On the basis of clinical examination, serological and radiological investigations, surgical management of patient was planned. Management included surgical procedure with or without radiological intervention. Surgical procedures were done in accordance with the standard treatment protocol. Data was compiled using a detailed proforma. After discharge patients were followed up at 3weeks, 6weeks and every 3months thereafter.

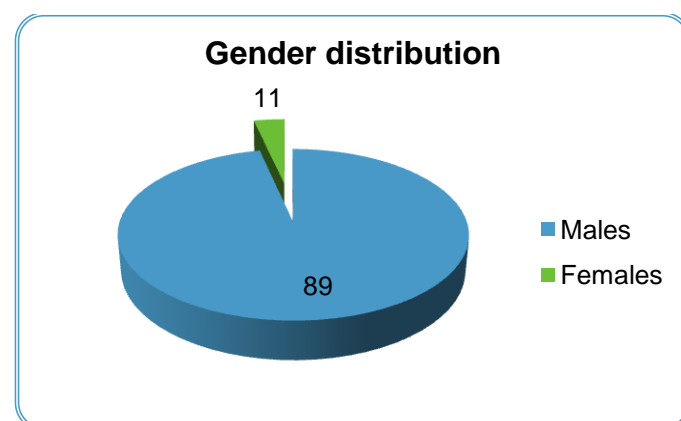
### Observations and Results

The study of surgical complications of pancreatitis revealed that the peak incidence of their occurrence was seen in between the age group of 30-39 years (29.54%) and minimum cases were seen in the age group of 0-9 years (2.27%).

**Table 1:** Incidence of surgical complications of pancreatitis in different age groups.

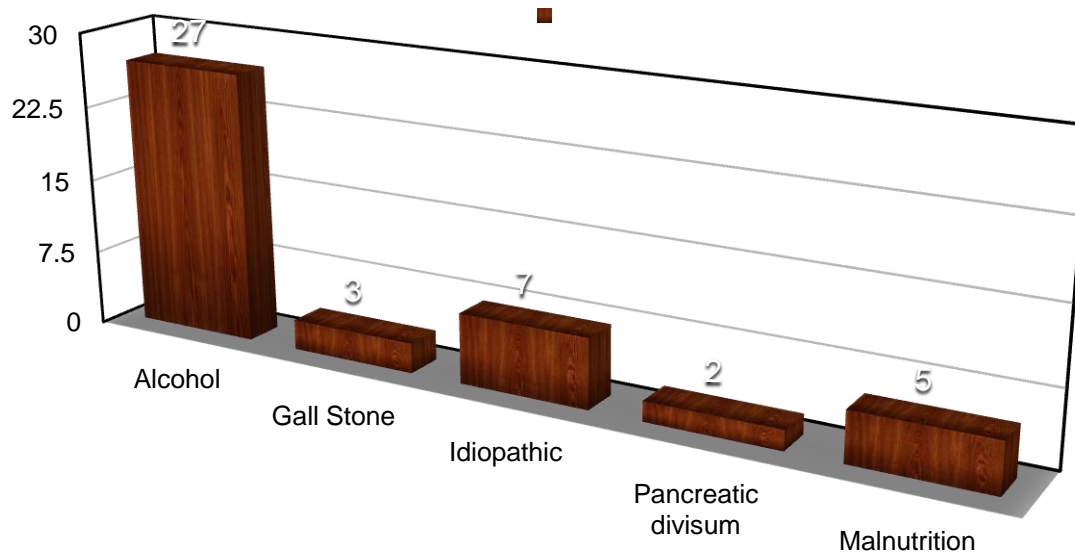
Age Groups (Years)	Number of subjects (%)
0-9	1 (2.27)
10 -19	4 (9.09)
20 – 29	11 (25)
30 – 39	13 (29.54)
40 – 49	7 (15.90)
50 – 59	5 (11.36)
>60	3 (6.81)
Total	44

The surgical complications of pancreatitis were predominantly seen in males with male to female ratio being 1:0.12.



**Fig 1:** Gender distribution of the studied cases.

The analysis of the etiological factor for surgical complication of pancreatitis revealed that alcohol (68.18%) was most common etiological agent associated with pancreatitis followed by idiopathic and tropical pancreatitis.



**Fig 2:** The analysis of studied cases according to etiological factor.

The most common chief complaint of the patient was pain (90.90%) followed by weight loss 86.36%, steatorrhoea in 43.18%, vomiting 40.90%, fever 18.18%, lump in abdomen 36.36%, yellowish discoloration of sclera 20.45%, Abdominal distention 13.63%, guarding 11.36%, tenderness 27.27%, breathlessness 15.90%, malena and hematemesis 4.54% of patients. Abdominal distention occurred in 4 cases of pancreatic necrosis and 2 cases of pancreaticopleural fistula. Yellowish discoloration of sclera occurred in total 9 cases out of which 3 cases were of chronic pancreatitis limited to head in which whipples procedure was done, 3 case were of chronic pancreatitis with dilated pancreatic duct and remaining 3 case were of pseudocyst of pancreas compressing CBD in which cystoenteric anastomosis were done. Lump in abdomen was presenting complaint and clinical examination finding in total 16 patients, out of which 10 were pseudocysts of pancreas, 5 patients were of pancreatic necrosis and 1 patient was of chronic pancreatitis limited to head of pancreas. Tenderness on abdominal examination was present in 12 cases out of which 5 patients were of pancreatic necrosis, 4 patients were of pancreaticopleural fistula and 3 patients were of infected pseudocyst. Guarding was present in all 5

patients of pancreatic necrosis. Breathlessness was present in 7 patients of pancreaticopleural fistula. Hematemesis and malena was present in postpancreatitis splenic vein thrombosis with portal hypertension with gastric varices.

**Table 2:** Presenting complaints in the studied cases

Complaints	Number of subjects (%)
Lump in abdomen	16 (36.36)
Abdominal distention	6 (13.63)
Guarding	5 (11.36)
Tenderness	12 (27.27)
Pain	40 (90.90)
vomiting	18 (40.90)
Fever	8 (18.18)
Icterus	9 (20.45)
Weight loss	38 (86.36)
Steatorrhoea	19 (43.18)
Breathlessness	7(15.90)
Hematemesis	2 (4.54)
Malena	2 (4.54)

The General examination of the patients revealed that the most common finding was raised pulse rate (70.45%) followed by icterus (20.45%) and raised temperature (18.18%). Hypertension was seen in 6 (13.63%) patients while hypotension was seen in 5 (11.36%) patients. The haematological investigations revealed that Serum bilirubin was raised in total 12 cases, out of which 9 cases had chronic pancreatitis was an etiology and 3 patients had gall stones. Serum lipase was raised in 31 cases of pancreatic necrosis (5), pancreaticopleural fistula (7) and pseudocyst of pancreas (16) and chronic pancreatitis with ductal dilatation (3).

**Table 3 :** Blood Investigations of the studied subjects.

<b>Haemoglobin</b>		
Values	< 10	> 10
No. of Subject	16	28
<b>TLC</b>		
Values	< 12000	>12000
No. of Subject	37	7
<b>Serum Billirunbin</b>		
Values	< 1.5 mg	>1.5 mg
No. of Subject	32	12
<b>BSR</b>		
Values	< 200	>200
No. of Subject	39	5
<b>Serum Lipase</b>		
Values	normal	raised
No. of Subject	13	31

Serum bilirubin was raised in total 12 cases, out of which 9 cases had chronic pancreatitis was an etiology and 3 patients had gall stones. Serum lipase was raised in 31 cases of pancreatic necrosis (5), pancreaticopleural fistula (7) and pseudocyst of pancreas (16) and chronic pancreatitis with ductal dilatation (3).

In surgical complications of pancreatitis patients, pleural effusion on chest x ray was seen in 29.54% patients and Calcification on X abdomen was seen in 27.27% cases. Out of 13 patients with pleural effusion, 7 patients had gross pleural effusion in which intercostal drain insertion was

done and remaining 6 patients had non tapable pleural effusion but was seen on chest X ray. Out of 12 patients of calcification, 9 patients had duct dilatation with ductal calculi and 3 patients had pancreatic head parenchymal calcification.

Out of 44 patients with Surgical complications of pancreatitis, 16 (36.36%) patient had pseudocyst, 11(25%) had pancreatic ductal dilation with or without ductal dilatation with or without obstructive jaundice, 5 (11.36%) patients of pancreatic necrosis and 8 (18.18%) patients of each of chronic pancreatitis limited to pancreatic head and 7 (15.90%) patients had pancreaticopleural fistula, 3(6.81%) patients of splenic vein thrombosis with gastric varices.

**Table 4:** Surgical complications of pancreatitis studied in this study.

Surgical Complications	No. of subjects (%)
Pseudocyst	16 (36.36)
Ductal dilatation with or without ductal calculi with or without obstructive jaundice.	11 (25)
Pancreatic Necrosis	5 (11.36)
Chronic pancreatitis limited to Pancreatic head	3 (6.81)
Pancreaticopleural fistula/ pancreatic pleural effusion.	7 (15.90).
Splenic vein thrombosis with gastric varices	2 (4.54)
Total	44

In surgical complications of pancreatitis, most common finding observed was chronic pancreatitis changes with pseudocyst formation in 36.36% of patients. Pancreas was found atrophic in 20.45% and calcification was seen in 27.27% of patients. Dilated MPD was seen in 25% and ductal calculi in 20.45%. Splenic vein thrombosis with portal hypertension with gastric varices was seen in 4.54% of cases, pseudocyst with intracystic bleeding was in 2(4.54%) patients, multiple pseudocysts in 6.81% patients& CBD dilatation due to distal CBD obstruction was found in 20.45% cases.



**Table 5: Radiological Imaging findings on Ultrasonography, CT scan and MRCP in Surgical Complications of Pancreatitis**

Finding	No. of subjects	
	Present	Absent
Atrophy of Pancreas	9 (20.45)	35 (79.54)
Pancreatic Calcification (ductal+ parenchymal)	12 (27.27)	32 (72.72)
Dilated MPD > 7 mm	11 (25)	33 (75)
Pancreatic Ductal Calculi only	9 (20.45)	35 (79.54)
Uncomplicated Pseudocyst	14 (31.81)	30 (68.18)
Pseudocyst with intra cystic bleeding	2(4.54)	42(95.46)
Multiple Pseudocysts	3(6.81)	41(93.19)
CBD Dilatation	9 (20.45)	35(79.54)
Splenic vein thrombosis with portal hypertension with gastric varices	2 (4.54)	42 (95.45)

7 Patients with retrogastric pseudocysts, cystogastrostomy was done. 1 patient with pseudocyst was near duodenum, cystoduodenostomy was done. 5 patients with pseudocysts compressing transverse mesocolon, cystojejunostomy was done. In 3 patients with multiple pseudocysts, cystoenteric anastomosis of largest cyst and intraoperative needle aspiration of other small cyst was done.

Out of 9 patients of obstructive jaundice, 3 patients had ductal calculi, 3 patients had chronic pancreatitis limited to head of pancreas and 3 patients had obstructive jaundice due to pseudocyst compressing distal common bile duct. Analysis of body mass index of the patients revealed that it was more than 18.5 in 88.63 % of patients preoperatively and serum albumin was more than 3 in 81.81% of patients.

Out of the patients who underwent surgical interventions the most common procedure done was intercostal drain for patients of pancreaticopleural fistulas or pancreatic pleural effusion with gross pleural effusion. Other common procedures done were Laparoscopic

cystogastrostomy, laparoscopic Longitudinal Pancreaticojejunostomy and Open Whipples procedure. Out of total 44 patients of surgical complications of pancreatitis, minimal invasive techniques that is laparoscopy was used in 16 (36.36%) patients. The details of all surgical procedures done in the studied cases is given in table.

**Table 6. Surgeries performed in Surgical Complications of Pancreatitis.**

Operations	No. of subjects(%)
Open Necrosectomy	3 (6.81)
Laparoscopic Necrosectomy	2 (4.54)
Open Cystogastrostomy	2 (4.54)
Laparoscopic cystogastrostomy	5 (11.36)
Open Cystoduodenostomy	1 (2.27)
Open cystojejunostomy	2 (4.54)
Laparoscopic cystojejunostomy	3 (6.81)
Pseudocyst external drainage	3(6.81)
Open Longitudinal Pancreaticojejunostomy (LPJ)	3(6.81)
Laparoscopic LPJ	4(9.09)
Open Beger procedure	1(2.27)
Open Berne procedure	1(2.27)
Laparoscopic Berne procedure	1(2.27)
Laparoscopic Frey procedure	1(2.27)
Open Whipples procedure	3(6.81)
Intercostal drain insertion	7 (15.90)
Splenectomy	2(4.54)
total	44

Laparoscopic surgeries have benefit of less morbidity and less hospital stay hence laparoscopic surgeries were performed whenever feasible Out of total 44 patients of surgical complications of pancreatitis, minimal invasive

techniques that is laparoscopy was used in 16 (36.36%) patients and open surgeries were performed in 28 patients (63.63%).

**Table 7:** Laparoscopic procedures done in studied cases.

Operation	Patients
Laparoscopic necrosectomy	2
Laparoscopic cystogastrostomy	5
Laparoscopic cystojejunostomy	3
Laparoscopic L.P.J.	4
Laparoscopic Berne procedure	1
Laparoscopic Frey procedure	1
Total	16

Immediate postoperatively before discharge, wound infection was seen in 9.09% of the patients, bleeding was seen in 4.54%, anastomotic leak in 4.54% of patients. Reactionary gastrointestinal bleeding occurred in 2 patients, out of which 1 was of whipples procedure where bleeding occurred near superior mesenteric artery and other was of cystogastrostomy where bleeding occurred at anastomotic site. Anastomotic leak occurred in one patient of whipples procedure and other of pancreaticojejunostomy.

**Table 8 :** Immediate postoperative complications.

	Present (%)	Absent (%)
Wound infection	4(9.09)	40 (90.90)
Bleeding	2 (4.54)	42 (95.45)
Anastomotic leak	2 (4.54)	42 (95.46)

The most common late complication seen late (After 6 weeks) were deranged blood sugar, intra-abdominal abscess and weight loss.

**Table 9 :** Late post-operative complications.

Complications	Present (%)	Absent (%)
Fistula formation	2 (4.54)	42 (95.45)
Pseudocyst recurrence	1 (6.25)	15(93.75)
Deranged blood sugar	5 (11.36)	39 (88.63)
Weight loss	3 (6.81)	41 (93.18)
Intra abdominal abscess	3 (6.81)	41 (93.18)

Out of 16 patients operated for pseudocyst, recurrence was seen in only 1 patient, out of 7 cystogastrostomy was done 1(14.28%) got recurrence of pseudocyst. Out of 6 patients underwent Puestow procedure, all 100% patients which underwent weight gain. Out of 3 patients of Berne, Begers and Frey procedure 66.66% patients got weight gain. Out of 7 patients of cystogastrostomy 71.42% patients underwent weight gain. Out of 3 patients of whipples procedure 100% patients had weight gain. Out of 5 patients of necrosectomy, only 20% patients had weight gain. Out of 6 patients underwent Puestow procedure, 83.33% underwent pain relief. Out of 3 patients of Berne, Beger and Frey procedure 66.66% patients got pain relief. Out of 7 patients of cystogastrostomy 85.71% patients got pain relief. Out of 3 patients of whipples procedure 66.66% patients had pain relief. Out of 5 patients of necrosectomy, only 20% patients had pain relief.

**Table 10 :** Mortality According to Operative Procedure

Surgical Procedure	Mortality(%)
Pseudocyst drainage	1 (6.25%)
Necrosectomy	2(40%)

Necrosectomy was done for pancreatic necrosis having highest mortality (40%). For pseudocyst drainage mortality is 6.25%.

Overall mortality of surgical complications of pancreatitis was 6.81%.

## Discussion

The present study shows that surgical complications of pancreatitis needing surgical intervention are seen at all age groups. The peak of incidence was seen in 30-39 years (29.54%) mean age group was 40.12 years ( $\pm 11.07$ ) Balakrishnan et al <sup>[11]</sup> is a study in 2008 observed mean age group of patients to be 39.7 years (SD  $\pm 14.1$ ). Tusia Sato et al <sup>[12]</sup> observed mean age of 45 years, and W Schosser et al <sup>[13]</sup> observed 45.8 years as mean age. Thus the results of our study correlate with these studies. In present study, patients with surgical complication of pancreatitis. Out of 44 patients studied 86.63% patients were males and 11.36% were female. Balakrishnan et al, in a study in 2008 found 79.26% were male and 20.74% were female. P. Kandasani et al 2002 <sup>[14]</sup> also found more common in males (76.3%) than females Alcohol was found predominant in about 60-80% of patients, idiopathic pancreatitis in 20%, hereditary, tropical and others form rest of the group. Another study by Ramesh Roop Rai et al <sup>[15]</sup> found alcohol intake as etiology in 59.5% of patients, idiopathic pancreatitis in 17.4%, rest patients had hereditary, traumatic and other etiologies. In study done by Wei-Xing Chen et al <sup>[16]</sup> in 2006 abdominal pain was Chief complaints in 81.7% of patients, 26.9% of patients presented with lump in abdomen, jaundice was seen in 12.76%. Many parameters in present study are comparable to Wei-Xing Chen et al.

In the present study, Ultrasound was done in all patients. Ultrasound was performed as the initial investigation at the time of admission to confirm the diagnosis by visualization of pancreas and also to look for gall bladder disease and peripancreatic collection. Ultrasonography aids in visualization of gall bladder calculi, dilation of common bile duct, gross edema of pancreas, abscess pseudocyst, ascites and peripancreatic fluid collection. Similar findings were reported by A.J. Mokay et al <sup>[17]</sup> in 2005. Grey scale reported by A.J. Mckay et al in 2005. Grey scale ultrasound is useful method of detecting gallstones in patients with acute pancreatitis, thus permitting early

accurate biliary surgery. In present study, CT scan done in all patients. Majority of the patients (36.36%) operated for pseudocyst. Out of total operated cases of pseudocyst, 14 (31.81) were uncomplicated, 2(4.54%) had intracystic hemorrhage and 3(6.81%) had multiple pseudocysts. Atrophy of pancreas was seen in 20.45% cases. Calcification (ductal+parenchymal) was seen in 27.27% of patients. Dilated MPD was seen in 25% and ductal calculi in 20.45%, postpancreatitis splenic in thrombosis with gastric varices in 4.54% of patients and CBD dilatation in 20.45% patients, due to distal obstruction. Various studies have similar findings as this present study has Eulatio <sup>[18]</sup> stated incidence of pseudocyst in alcohol related chronic pancreatitis is 56-78% of patients. In present study out of 16 patients operated for pseudocysts, 43.75% patients were operated as cystogastrostomy which were retrogastric in location. In 31.25% cases cystojejunostomy was done in which pseudocysts were located near transverse mesocolon. In 6.25% cases cystoduod-enostomy was done in which pseudocyst was located near duodenum. These findings match with study by Gang Pan et al <sup>[19]</sup> in 2015. In present study 6.81% patients operated for whipples and 9.09% patients operated for duodenum preserving pancreatic head resection (DPPHR)

Similar findings were from study of Buchler MW et al <sup>[20]</sup> in which whipple procedure was done in 10.45% and DPPHR was done in 15.78% of patients. In present study longitudinal pancreaticojejunostomy was done in 15.90% of patients. In study of Beger et al <sup>[21]</sup>, longitudinal pancreaticojejunostomy was done in 10-15% of cases. In present study out of 7;4 done laparoscopically. Overall results post operative were excellent with laparoscopic surgery over open technique except for increased operative time and technical difficulty requiring skillful surgeon.

Different resection, drainage and hybrid surgical procedure was done for chronic pancreatitis limited to head of pancreas with or without CBD obstruction like Whipples procedure, Beger



procedure, Berne procedure, Frey procedure. Out of 4 patients of Berne, Beger and Frey Procedure, 3 patients gained weight and pain relief.

In study by Choon-Kiat Ho et al <sup>[22]</sup>, showed that organ preserving procedures for chronic pancreatitis such as Frey, Beger combines good efficacy for pain relief with low surgical morbidity and mortality in 75-80% cases.

In present study, bleeding and anastomotic leak and wound infection found in 4.54% and 9.09% patients respectively. These findings nearly matches with study was done by Choon-Kiat HO et al in which, bleeding and anastomotic leak was found 3-13% and 0-13% patients respectively. In this study late complications like fistula formation, intra-abdominal abscess, deranged blood sugar levels and formation of pseudocyst was comparable to studies conducted by Newell KA et al <sup>[23]</sup> Volker Keim et al <sup>[24]</sup>.

### Conclusion

In this study it has been found that surgical complications of pancreatitis requiring surgical interventions like pseudocyst of pancreas, pancreatic necrosis etc. can be effectively managed by surgical interventions.

These surgical interventions can be performed effectively by open and laparoscopic procedures. Laparoscopic approach should preferred for pancreatic surgeries as having less post operative complications and patients satisfaction.

In complications of pancreatitis, surgical management is preferred modality in terms of better prognosis, pain relief and weight gain. Also it shows overall increased survival of the patients.

Conflict Of Interest: None

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