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INFECTED ACUTE PANCREATIC NECROSIS AFTER ACUTE PANCREATITIS: A RETROSPECTIVE STUDY

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Abstract:

Acute pancreatitis is an inflammatory disease that changes from mild interstitial edema of the pancreas to extreme type of pancreatic necrosis and hemorrhage. In this study, frequency and in the development of infected pancreatic necrosis after acute pancreatitis were noted. A total of 105 patients [Male and Female] with age range 40-75 year were included in this study. A random sampling technique [95% confidence level] was used for a reliable statistical conclusion. Demographic history was obtained from the patient's records included in this study and their files were reviewed including an abdominal CT scan to check for pancreatic necrosis and CT-guided fine-needle aspiration cytology [FNAC] to verify infection. Prevalence of infected acute pancreatic necrosis among the patients of severe acute pancreatitis was n=34/105 i.e 32% of the total patients. The main contributing factors in developing the infective pancreatic necrosis are choledocholithiasis, gallstones, hypercalcemia, idiopathy, pancreatic or ampullary tumors, trauma, and hypothermia respectively.

Keywords: *Infection, severe acute pancreatitis, CT, Ranson, gall-stone, idiopathic.*

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INTRODUCTION

In acute pancreatitis, within 14 days, inflammatory mediators are released which lead to systemic inflammatory response syndrome [SIRS].[1] In the absence of infection, organ dysfunction as well as other disorders, such as increased permeability of capillary, hypovolemia, fluid loss from the intravascular space and hyperdynamic circulatory regulation, occurs. In the second phase, after two weeks of beginning of the disease, infection of pancreatic necrosis leads to sepsis-related complications. [2]

Severe acute pancreatitis [SAP] is characterized as an AP connected with systemic complications. This classification is a clinically based group characterizing AP complications and severity. Failure in organ functioning within 72 h of the onset is characterized as an early severe acute pancreatitis [ESAP]. ESAP is characterized is by an increasing MODS, short course, early hypoxemia, expanded rate of malfunction of abdominal compartment disorder [ACS]. Pancreatic necrosis, multiorgan dysfunction syndrome, sepsis, and infection, cause the mortality in acute pancreatitis. Necrosis in the pancreas causes infection which becomes the main reason of late mortality. Renal failure [RF], cardiovascular [CVF] and acute respiratory failure [ARF], can forecast the deadly result in severe acute pancreatitis. [3] Most of the mortalities [20-40%] have been reported due to severe acute pancreatitis. In acute pancreatitis, premature activation of pancreatic enzymes inside the pancreas leads to autodigestion of the gland and inflammation. The pancreatic enzymes enter the bloodstream and stimulate the production of inflammatory tumor necrosis factor-α [TNF- α] and inflammatory cytokines. Due to the release of the pancreatic enzymes, it triggers an inflammatory flow leading to systemic inflammatory response syndrome. Correct diagnosis of severe acute pancreatitis at the time of hospital admission, quick SAP characterization is of great importance.

Necrotizing pancreatitis leads to high mortality rate causing 40-70% deaths. [4] Due to complications caused by this debilitating disease nearly one half of the patients die due to necrotizing pancreatitis & approximately 30% of patients die with superadded infection. While non necrotizing acute necrotizing pancreatitis causes deaths only in 10-15% of patients. [5] In the 1980s three patterns evolved for the surgical treatment of necrotic acute and infective pancreatitis. These involved necrosectomy, lavage, and laparostomy [open abdominal management]. [6]

There are many causes of acute pancreatitis but most common are excessive the use of excessive alcohol consumption or the presence of gallstone. Frequency of acute pancreatitis varies geographically. Common causes in the United Kingdom and Asia are due to gallstones, while in the USA and Finland most causative agent is alcohol consumption. The idiopathic group still consists of 10-30% cases. Interest is focused on biliary sludge, as reported it is present in 70% of patients suffering from acute pancreatitis with idiopathic acute pancreatitis. While the rest of the 10% cases are of miscellaneous etiologies and there are many different kinds of inducing agents. [7]

Most of the deaths occur due to complications like infection of pancreatic necrosis. Previous studies have found an important link between acute pancreatitis and genetic factors, but studies involved comparatively small cohorts. All these data showed a positive link between recurrent and acute pancreatitis. Malfunction gastrointestinal mucosal barrier is present because it allows translocation of bacteria that leads to severe inflammation, infection and many other complications. Few reports are available about the reason and physiology of failure in the mucosal barrier in the case of acute pancreatitis that may lead to the initiation of this disease. Failure in tight junction within the pancreas may be an important reason for the early development of acute pancreatitis. [8]

Gallstones and alcohol misuse are the main and important reasons for acute pancreatitis. During the past 20-30 years, however, the risk of biliary pancreatitis is unlikely to be more than 2% in patients with asymptomatic gallstones and that of alcoholic pancreatitis is unlikely to exceed 2–3% in heavy drinkers. Other factors are genetic and therefore probably play their part. Indiscriminate use of drugs is also one of the important reason for acute pancreatitis.

Other etiologic factors include infectious diseases, traumatic acute pancreatitis, and hyperparathyroidism. The rationale for this study was the absence of any report about the frequency and the contributing factors in the development of infected pancreatic necrosis after severe acute pancreatitis in our setting.

MATERIALS AND METHODS:

This study was conducted in the surgical floor of Mayo Hospital, Lahore, Pakistan.
Design: Retrospective study

Inclusion criteria: All patients with severe acute pancreatitis established with Revised Atlanta classification [annexure attached], of both genders, aged 21-80 years, were included. Ranson score was > 3.

Exclusion criteria: Patients with recurrent or chronic pancreatitis [history of pain and positive CT scan findings], malignancy [on CT scan abdomen and biopsy], diabetes mellitus [Two Fasting BSL readings>125mg/dl or one random BSL>200mg/dl], and primarily treated at another hospital was excluded.

Patients presented the surgical floor of Mayo Hospital Lahore, fulfilling inclusion and exclusion criteria were included after reviewing the records. Demographic history was obtained from the files. Patient history and investigations along with their progress was reviewed from the notes. Data were collected by the researcher himself and recorded in a predesigned Performa.

Data were entered and analyzed using IBM SPSS Statistics version 21 software. Continuous variables, such as age and Ranson score were described by mean [±SD] or median and categorical data like gender, infected pancreatic necrosis and contributing factors like gallstones, chronic alcohol consumption, choledocholithiasis, hypercalcemia, hypothermia, idiopathic, tumors and trauma were presented in frequency and percentages.

RESULTS:

In the present study, a total of 105 cases were enrolled. The mean age of the patients was 49.67±16.99 years with minimum and age ranged 21-80 years. 71 [67.62%] patients were males and 34 [32.38%] were females. The male to female ratio was 2.1:1. The CT necrosis was absent in 34 [32.4%] patients and < 30% necrosis was detected in 28 [26.7%] cases, while 30-50% necrosis was recorded in 18 [17.1%] cases and > 50% necrosis was found in 25 [23.8%] cases using the CT scan for necrosis.

Fever was observed only in 78 [74.3%] cases and it was not observed in 27 [25.7%] cases. The results also revealed the incidence of leukocytosis in 79 [75.2 %] cases and it was not noted in 26[24.8%] cases. Abdominal pain was reported by 72.38% patients and it was not found in 27.63% patients. Bacterial culture was found to be positive in 37 [35.2%] patients, while it was negative in 68 [64.8%] patients. The fungal culture was noted positive in 34 [35.2%] patients only and it was noted negative in 71 [67.6%] patients. The gall stones were present in 41 [39.0%] cases and were absent in 64 [61.0%] cases. In this study, traumatic conditions were found in 32.38% of patients and it was not found in 67.62% patients.

DISCUSSION:

The objective of the study was to determine the frequency of infected pancreatic necrosis among patients and compare the frequency of contributing factors among acute pancreatitis patients with infected pancreatic necrosis. The study showed that the most vulnerable age for pancreatitis was 21-80 years. This wide range indicates that age is not an important factor contributing to pancreatitis. However, the study suggests that gender may be an important factor where the ratio of female to male patients is almost 1:2 [Figure 2.1]. This ratio may be due to many reasons some of which are outlined as Gallstones, Certain medications, Cigarette smoking, Cystic fibrosis, Family history, Alcohol consumption and Hormonal changes[10].

Although gallstones are more common in females than males, [11] our study showed the opposite ratio i.e 2:1 in favor of males. Approximately 80% of all cases can be attributed to either gallstones or alcohol [12]. The frequency of different forms of acute pancreatitis varies markedly in different countries. Gallstones are the most common cause in the United Kingdom and Asia, whereas, in the USA and Finland, alcohol is the most common causative factor. [13, 14]Cigarette smoking cannot be excluded in higher pancreatitis frequency in males than females. [13]

Necrosis in pancreatitis patients is the second stage of pathology in this disease. [15] In the present study, it was observed that necrosis was 26.7% in 28 patients who had less than 30% necrosis on CT scan. This indicates that in most patients, pancreatitis can be cured without experiencing necrosis. Table 2.2 shows that 30-50% of the pancreatitis necrosis commonly take place in 17.1% of severe acute pancreatitis while >50% necrosis was as high as 23.8%. The table concludes that pancreatitis if left unattended, results in a high rate of necrotic tissue. In necrotizing pancreatitis, the most important risk factor resulting in death is infection of pancreatic necrosis which occurs in 40 to 70% of patients[16]. Beger and coworkers [17] have found a fourfold increase in mortality [37.8% v 8.7%] in patients with infected necrosis. Although 47% of the total patients with pancreatic necrosis have positive bacteriology.

Necrosis may follow infection leading to fever. Table 5.3 shows that 74.3% of the patients had fever compared with 25.7% normal body temperature. This

indicates that infection is a commonplace in severe acute pancreatitis patients. This is confirmed with a higher percentage of leukocytes in 75.2% patients compared with only 24.8% of patients with normal leukocytes count. A high necrotic rate, higher leukocyte [Infection] count explains abdominal pain in 72.38% of the patients shown in while 27.62% of patients were normal.

Infection may be bacterial, fungal or viral. If severe acute pancreatitis patients are left untreated, necrosis followed by infection is an obvious endpoint. Table 5.5 shows that 35.2% of patients of the sevre acute pancreatitis patients had bacterial infection while 64.8% were without bacterial infection. [18, 19] This percentage is similar to fungal when viral infection is also taken into account.

Gallstones cause obstruction of the cystic and common bile ducts hindering bile circulation and resulting in hepatic injury. [20] This is shown by hepatic enzymes leakage out into the blood indicating hepatic injury. In the present study, 39.0% of the severe acute pancreatitis patients were suffering from gallstones indicating that these are one of the major causes of pancreatitis and should be treated as soon as they present with symptoms. Choledocholithiasis i.e stone in common bile duct is a separate risk factor for developing severe acute pancreatitis as it was present in 30% of patients and all of these went on to develop infective pancreatic necrosis.

Alcohol consumption is a known hepatic injury inducer leading to severe acute pancreatitis. [14] In the present study, 23.8% of the alcoholic patients suffered severe acute pancreatitis which is 50% less than the gall stones indicating gallstones are a more important cause of pancreatitis. Hypercalcemia *per se*, in addition to being an independent risk for the precipitation of pancreatic cellular injury, could also augment pancreatic disease in patients with ongoing pancreatic injury because of other causes and thus leads to severe acute pancreatitis [21, 22] In the present study 34.3% of the patients were suffering from hypercalcemia.

Hypothermia may be caused by sepsis in the elderly. If necrosis occurs followed by infection and sepsis, hypothermia is an evident result. [23] In the present study, 29.5% of the patients suffered hypothermia suggesting that the infection had ensued in these patients and rapid treatment with antibiotics must be taken on priority. Idiopathic causes may also be important in pancreatitis patients. For example, idiopathic polyneuritis, idiopathic pulmonary fibrosis, idiopathic scoliosis are important etiologies for severe acute pancreatitis patients. [24] One study has revealed that between 10 to 35% of the total cases of acute pancreatitis may be idiopathic in nature. African Americans have the highest age- and sex-standardized incidence rate of idiopathic pancreatitis [25]. Although controversial, many authorities recommend cholecystectomy for recurrent episodes of otherwise idiopathic pancreatitis associated with biliary sludge [26].

Table 1.1: Computed Tomography Severity Index

Fluid Collections	**Points**
Normal pancreas	0
Gland enlargement	1
Peripancreatic inflammation	2
One fluid collection	3
Multiple fluid collections	4
Necrosis	
<30%	2
30–50%	4
>50%	6
Total	10
CT severity index	Score
Low degree	0-3
Middle degree [6% mortality]	4-6
High degree [17% mortality]	7-10

Table 2.1: Descriptive statistics of age [years]

Age [years]	**N**	105
	Mean	49.67
	±SD	16.99
	Minimum	21
	Maximum	80

Table 2.2: Frequency of necrosis detected by CT scan

		# Patients	**%age**
Necrosis detection by CT scan	**Absent**	34	32.4
	< 30%	28	26.7
	30 - 50%	18	17.1
	50%	25	23.8
	Total	**105**	**100.0**

Table 2.3: Frequency of fever distribution

		# Patients	**%age**
Fever	**P**	78	74.3
	A	27	25.7
	Total	**105**	**100.0**

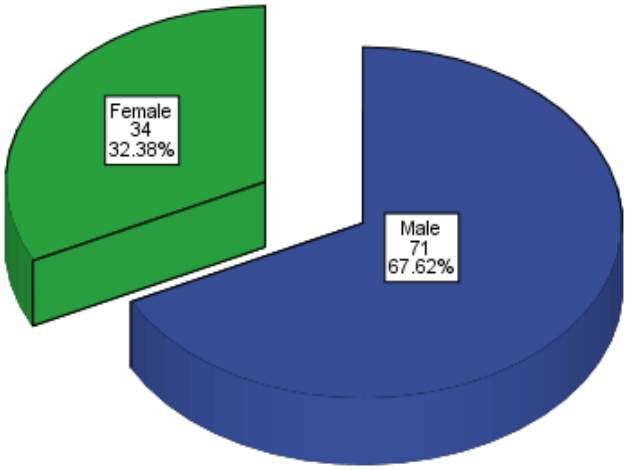

Figure 2.1: Frequency distribution by gender

Table 2.4: Frequency of Leukocytosis

		# Patients	**%age**
Leukocytosis	**P**	79	75.2
	A	26	24.8
	Total	**105**	**100.0**

P = Present; A = Absent

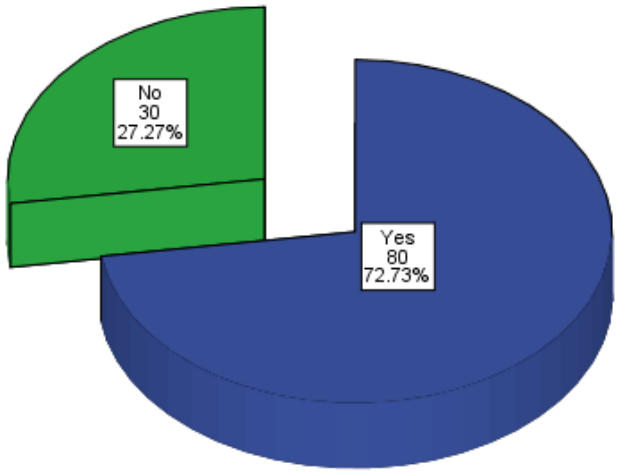

Figure 2.2: Frequency distribution of abdominal pain

Table 2.5: Frequency of bacterial culture

		# Patients	%age
Bacterial Culture	**+ve**	37	35.2
	-ve	68	64.8
	Total	**105**	**100.0**

Table 2.6: Frequency of fungal culture

		# Patient	%age
Fungal culture	**+ve**	34	32.4
	-ve	71	67.6
	Total	**105**	**100.0**

Table 2.7: Frequency of gall stone

		# Patient	%age
Gall stone	**P**	41	39.0
	A	64	61.0
	Total	**105**	**100.0**

P = Present; A = Absent

Table 2.8: Frequency of chronic alcohol consumption

		# Patients	%age
Chronic alcohol Consumption	**P**	25	23.8
	A	80	76.2
	Total	**105**	**100.0**

P = Present; A= Absent

Figure 2.3: Frequency of choledocholithiasis

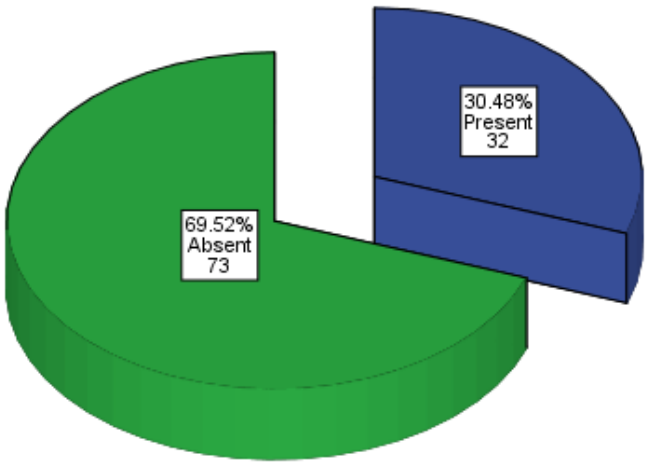

Table 2.8: Frequency of chronic alcohol consumption

		# Patients	%age
Chronic alcohol Consumption	**P**	25	23.8
	A	80	76.2
	Total	**105**	**100.0**

P = Present; A= Absent

Table 2.9: Frequency of hypercalcemia or hyperparathyroidism

		# Patients	%age
Hypercalcemia, Hyperparathyroidism	**P**	36	34.3
	A	69	65.7
	Total	**105**	**100.0**

P = Present; A = Absent

Table 2.10: Frequency of hypothermia

		# Patients	%age
Hypothermia	**P**	31	29.5
	A	74	70.5
	Total	**105**	**100.0**

P = Present; A = Absent

Table 2.11: Frequency of idiopathy

		# Patients [no.]	%age
Idiopathy	**P**	36	34.3
	A	69	65.7
	Total	**105**	**100.0**

P = Present; A = Absent

Table 2.12: Frequency of pancreatic or ampullary tumors

		# Patients	%age
Pancreatic or ampullary tumors	**P**	45	42.9
	A	60	57.1
	Total	**105**	**100.0**

P = Present; A = Absent

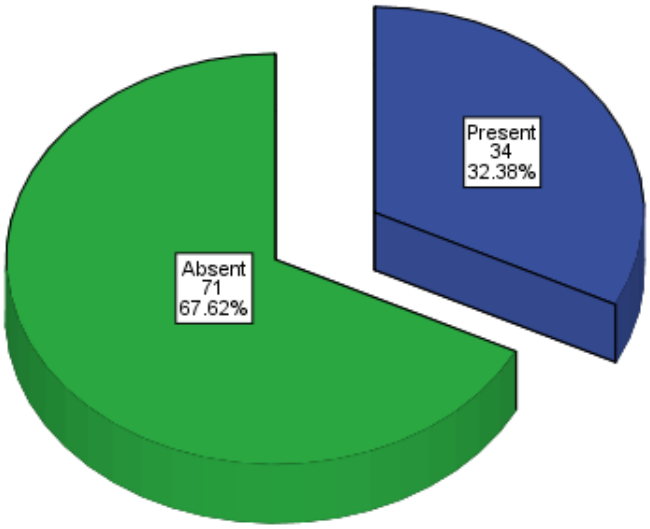

Figure 2.4: Frequency of trauma

Table 2.13: Comparison of infection in cases with different levels of pancreatic necrosis

		Infections		Total
		Present	Absent	
Pancreatic necrosis	Absent	2	32	34
	<30% necrosis	9	19	28
	30-50% necrosis	11	7	18
	>50% necrosis	10	15	25
Total		32	73	105

Table 2.14: Comparison of IPN with different causes

		Infective necrosis		p-value
		Present	Absent	
Gallstone	Present	16	25	0.128
	Absent	16	48	
Chronic alcohol consumption	Present	7	18	0.758
	Absent	25	55	
Choledocholithiasis	Present	32	0	0.000
	Absent	0	73	
Hypercalcemia, hyperparathyroidism	Present	14	22	0.176
	Absent	18	51	
Hypothermia	Present	7	24	0.255
	Absent	25	49	
Idiopathy	Present	14	22	0.176
	Absent	18	51	
Pancreatic or ampullary tumors	Present	13	32	0.760
	Absent	19	41	
Traumatic	Present	10	24	0.870
	Absent	22	49	

CONCLUSION:

Around one third of the patients of acute pancreatitis had infected acute pancreatic necrosis. Choledocholithiasis, hypercalcemia, pancreatic or ampullary tumors, trauma, and hypothermia were the important risk factors.

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