

Bacteriology of Infection in Severe Acute Pancreatitis

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ABSTRACT

Context Severe acute pancreatitis is associated with high mortality with infectious complications being the most common cause of mortality. **Objective** To analyze the prevalence and characteristics of pancreatic and extrapancreatic infection in patients with severe acute pancreatitis. **Design** Prospective study over a one-year period. **Patients** Fifty-one consecutive patients with severe acute pancreatitis. **Setting** Tertiary care centre, Northern India. **Main outcome measures** The presence of pancreatic and extrapancreatic infections were noted in consecutive patients with severe acute pancreatitis and their effect on disease outcome was assessed. **Results** Pancreatic infection was noted in 19 (37.3%) patients; 14 (27.5%) patients had monomicrobial and 5 (9.8%) patients had polymicrobial infections. In the first week of hospitalization, all positive 6/6 (100%) cultures grew *Escherichia coli*, in the second week 5/8 (62.5%) grew *Escherichia coli* while after the second week, 2/5 (40.0%) cultures grew *Escherichia coli*. A total of 32 (62.7%) patients had evidence of extrapancreatic infections, with 53 positive cultures. Fifteen (29.4%) patients had monomicrobial infections while 17 (33.3%) had polymicrobial infections. The most common site was blood together with intravenous site with 21 positive cultures in 16 patients. *Staphylococcus aureus* was most commonly isolated in the blood cultures. There was a statistically significant increase in mortality with pancreatic (P=0.003) and extrapancreatic (P=0.041) infections. The antibiotic sensitivity pattern showed that most of the bacteria were sensitive to beta lactum antibiotics, aminoglycosides and imipenem. **Conclusion** Pancreatic infections are more often monomicrobial with a shift from gram-negative to gram-positive as the pancreatitis progressed. Extrapancreatic infections are more often polymicrobial; most commonly, the blood stream is invaded by gram-positive bacteria.

INTRODUCTION

Acute pancreatitis is an acute inflammatory process of the pancreas with variable involvement of other regional tissues or remote organ systems. Infected pancreatic necrosis and pancreatic abscess are the most devastating of the complications leading to secondary pancreatic infections. Infectious complications are observed in 40-70% of all patients with severe acute pancreatitis [1, 2, 3]. Today most deaths related to acute pancreatitis occur after the first 7 to 10 days as a result of infective complications, particularly infected pancreatic necrosis [4, 5, 6, 7]. The infection rate correlates with the extent of the pancreatic necrosis and the bacterial contamination of the pancreatic necrosis, determines the course of the disease and patient outcome [5]. Pancreatic necrosis in the presence of

severe or prolonged systemic complications, if sterile, has a mortality rate of 20% while, in the case of infected necrosis, it increases to more than 50% [8]. Infected necrosis is associated with a high incidence of organ failure irrespective of the extent of the necrosis [8]. There is evidence that the bacteria originate from the gastrointestinal tract [9]. These patients are often given prophylactic antibiotics but there are reports that the use of this strategy may result in the development of an infection with resistant bacteria or fungi [10]. Patients with severe pancreatitis often require prolonged hospitalization and multiple interventions. They often have extrapancreatic infections which may also influence the outcome. However, there are only a few studies in the literature regarding the occurrence of extrapancreatic infections and their microbiological spectrum. We conducted this study to evaluate the prevalence and characteristics of pancreatic and extrapancreatic infections in patients with severe acute pancreatitis and to determine their effect on patient outcome. An additional objective was to look at the sensitivity pattern of the cultured microorganisms.

MATERIAL AND METHODS

This study involved 51 consecutive patients (40 males, 11 females; mean age 41.8±15.3 years) with severe

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Key words Pancreatitis, Acute Necrotizing; Bacterial Infections; Bacteremia

Abbreviations CTSI: CT severity index

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Table 1. Patient characteristics.

Total number of patients	51
Age; years (Mean±SD)	41.8±15.3
Gender:	
- Males	40 (78.4%)
- Females	11 (21.6%)
Duration of hospitalization; days (Mean±SD)	30.3±20.3
Etiology:	
- Alcohol	21 (41.2%)
- Gallstones	17 (33.3%)
- Drug induced	1 (2.0%)
- Hypercalcemia	1 (2.0%)
- Post traumatic	1 (2.0%)
- Idiopathic	10 (19.6%)
CECT necrosis:	
- <30 %	6 (11.8%)
- 30-50%	20 (39.2%)
- >50%	25 (49.1%)

CECT: contrast-enhanced computed tomography

acute pancreatitis seen by us over a one-year period in the Department of Gastroenterology of the Post-graduate Institute of Medical Education and Research, a tertiary care referral centre at Chandigarh, India. Patients above eighteen years of age with their first attack of severe acute pancreatitis were included in the study. The diagnosis of acute pancreatitis was made based on clinical features, elevated serum amylase and/or lipase levels (more than 3-fold the upper reference limit) and evidence of pancreatitis on contrast-enhanced computed tomography (CECT) of the abdomen. Severe acute pancreatitis was diagnosed if the patient had organ failure according to the Atlanta criteria [11], the CT severity index (CTSI) greater than 6 [12], the APACHE-II score greater than 8 and, when available, the Ranson score greater than 3 [13, 14]. Patients with known chronic pancreatitis or previous surgery for pancreatic disease were excluded from the study.

Table 1 gives patient characteristics. The most common etiology was alcohol followed by gallstones and other causes. The APACHE II score ranged from 9-10 in 28 patients (54.9%), 11-20 in 20 patients (39.2%) and 21-30 in 3 patients (5.9%). The CTSI ranged from 7-10: 20 patients (39.2%) had a CTSI of 10, 10 patients (19.6%) had a CTSI of 9, 15 patients (29.4%) had a CTSI of 8, and 6 patients (11.8%) had CTSI of 7. The Ranson score could be calculated in only three patients as the majority of the patients presented more than 48 hours after the onset of the acute pancreatitis. It was 4 in two patients (66.7%) and 3 in one patient (33.3%) of the 51 patients with severe acute pancreatitis studied.

All patients underwent analysis of hematocrit, total and differential blood counts, liver function tests, blood urea nitrogen and serum creatinine, blood gas analysis, blood sugar, serum calcium, coagulation profile and imaging consisting of a chest X-ray, an abdominal X-ray, and ultrasound and CECT of the abdomen.

All patients were closely monitored for pancreatic and extrapancreatic infections. Samples were taken for

culture from the blood, urine, throat, intravenous cannula tip, urinary catheter tip, tracheal aspirate (in those on a ventilator), drain fluid (if instituted) and bile (if drained). The culture media used were bile broth and trypticase-soy broth. Samples were taken at presentation, at 1 week, at 2 weeks and when the patient had a fever and/or leukocytosis. Pancreatic tissue was obtained either by ultrasound/CT guided fine needle aspiration (FNA) of the pancreatic necrotic tissue/peripancreatic collection or during surgery, and sent for bacteriological culture and gram staining in patients with suspected pancreatic infection. Tissue samples from patients undergoing necrosectomy were homogenized in a mechanical homogenizer before culture.

All patients were managed with prophylactic broad-spectrum antibiotics, parenteral/nasojejunal feeding, fluid and electrolyte management and supportive care with close monitoring. Patients admitted directly to the unit were given ciprofloxacin and metronidazole while those transferred from other hospitals continued the antibiotics they were already receiving. Indications for necrosectomy were: i) documented infected necrosis on culture, ii) worsening clinical condition and iii) persistent organ failure despite supportive care. Antibiotics were modified as per the sensitivity report. The patients were followed up until death or discharge from the hospital.

ETHICS

The protocol for the study was approved by the Ethical Committee of our institution, and written informed consent was obtained from all patients. The study protocol conforms to the ethical guidelines of the "World Medical Association Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects" adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964, as revised in Tokyo 2004.

STATISTICAL ANALYSIS

The prevalence, spectrum and antibiotic sensitivity of bacterial infections were compiled and expressed as percentages. All quantitative variables were expressed as mean±SD. The association of pancreatic and extrapancreatic infections with the extent of the necrosis and clinical outcome was determined using the linear-by-linear chi-square test and the Fisher's exact test when ordinal and dichotomic variables were involved, respectively. The frequencies of pancreatic and extrapancreatic infections were compared by means of the McNemar test. A two-tailed P value of less than 0.05 was considered significant. Statistical analysis was carried out using the statistical software package SPSS version 17.0 (SPSS, Chicago, Illinois, USA).

RESULTS

Pancreatic infection was documented in 19 (37.3%) out of the 51 patients. The fine needle aspirate taken from

Table 2. Microorganisms isolated in pancreatic and extrapancreatic infections in 51 patients with severe acute pancreatitis.

	Pancreatic infection	Extrapancreatic infection
Total positive cultures	22	53
<i>Escherichia coli</i>	13 (59.1%)	11 (20.8%)
<i>Staphylococcus aureus</i>	1 (4.5%)	10 (18.9%)
<i>Enterococcus faecalis</i>	2 (9.1%)	9 (17.0%)
<i>Acinetobacter baumannii</i>	1 (4.5%)	9 (17.0%)
<i>Pseudomonas aeruginosa</i>	3 (13.6%)	4 (7.5%)
<i>Klebsiella pneumoniae</i>	2 (9.1%)	2 (3.8%)
<i>Enterobacter aerogenes</i>	0	3 (5.7%)
<i>Alcaligenes xylosoxidans</i>	0	3 (5.7%)
<i>Morganella morganii</i>	0	1 (1.9%)
<i>Proteus mirabilis</i>	0	1 (1.9%)

the pancreatic tissue was positive in 14 patients and the culture of pancreatic tissue obtained at surgery was positive in 8 patients, with both being positive in 3 patients. Of the 22 positive pancreatic cultures, 19 (86.4%) grew gram-negative organisms while only 3 (13.6%) grew gram-positive organisms. All patients having both a positive fine needle aspirate culture and a positive culture of the operative tissue had identical organisms. Fourteen (73.7%) of the 19 patients had monomicrobial and 5 patients (26.3%) had polymicrobial infections. Table 2 gives a list of organisms cultured from the pancreatic tissue. There was a positive significant association between pancreatic infection and the degree of pancreatic necrosis: pancreatic infection was present in 1/6 (16.7%) patients with <30% necrosis, in 4/20 (20.0%) patients with 30-50% necrosis and in 14/25 (56.0%) patients with >50% necrosis (P=0.013). Of the 19 patients with pancreatic infection, 6 (31.6%) had infection in the first week of hospitalization, 8 (42.1%) in the second week and 5 (26.3%) in the third week or later. In the first week of hospitalization, all positive 6/6 (100%) cultures grew *Escherichia coli*, 5/8 (62.5%) grew *Escherichia coli* in the second week while 2/5 (40.0%) cultures were positive for *Escherichia coli* after the second week (P=0.036; Figure 1).

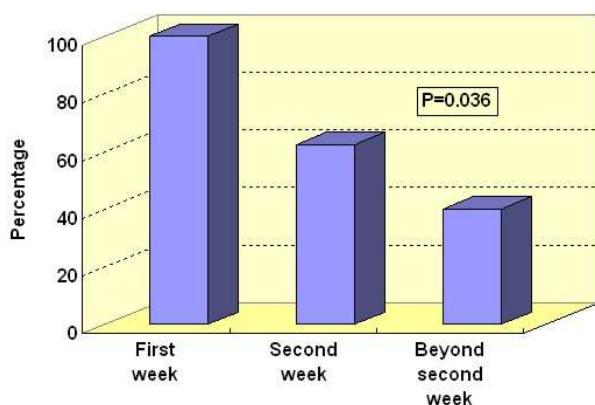


Figure 1. Proportion of infections caused by *Escherichia coli* out of all bacterial infections in 51 patients with severe acute pancreatitis. Data are given in percentages.

A total of 32 (62.7%) patients had evidence of extrapancreatic infections, with 53 positive cultures. The number of extrapancreatic infections was significantly higher than pancreatic infections (P=0.021) and there was no association between the presence of the two infections (P=1.000); in fact, 12 (23.5%) cases had no infection; 12 (23.5%) cases had both infections; 7 (13.7%) cases had pancreatic infections only; and 20 cases had extrapancreatic infections only. Of the 53 positive cultures, 19 (35.8%) were present in the first week, 9 (17.0%) in the second week and 25 (47.2%) after the second week. Fifteen of the 32 patients (46.9%) had monomicrobial infections while 17 (53.1%) had polymicrobial extrapancreatic infections. Table 3 gives the source of the 53 positive cultures. The most common site of extrapancreatic infection was the blood together with the intravenous site with 21 cultures (39.6%) in 16 patients; eight (38.1%) of these 21 cultures were positive in the first week, 5 (23.8%) in the second week and 8 (38.1%) after the second week. Overall, 37 (69.8%) organisms were gram-negative and 16 (30.2%) were gram-positive.

Twenty-one organisms were isolated in patients with a positive blood culture: *Staphylococcus aureus* was the most common organism (n=6; 28.6%) followed by *Escherichia coli* (n=4; 19.0%), *Enterobacter aerogenes* (n=3; 14.3%), *Alcaligenes xylosoxidans* (n=2; 9.5%), *Enterococcus faecalis* (n=2; 9.5%), *Pseudomonas aeruginosa* (n=2; 9.5%), *Acinetobacter baumannii* (n=1; 4.8%), and *Klebsiella pneumoniae* (n=1; 4.8%). Gram-negative bacilli were most commonly isolated in patients with a positive nasobiliary drain culture, pleural fluid culture and abdominal drain fluid culture (Table 4).

Table 5 gives the sensitivity pattern of organisms isolated from the pancreatic tissue and the extrapancreatic sites of the 51 patients. The antibiotic sensitivity pattern showed that the majority of the bacteria were sensitive to beta lactum antibiotics, aminoglycosides and imipenem.

Out of 51 patients, 29 (56.9%) were managed conservatively while 22 (43.1%) underwent surgery. Of these, 15 (68.2%) underwent an exploratory laparotomy and pancreatic necrosectomy whereas 7 (31.8%) underwent an exploratory laparotomy, pancreatic necrosectomy and lesser sac drainage. In 9

Table 3. Sites of 53 extrapancreatic infections found in 51 patients with severe acute pancreatitis.

Site	No. of cases (%)
Blood culture	16 (30.2%)
Intravenous site culture	5 (9.4%)
Urine culture	7 (13.2%)
Tracheal aspirate culture	5 (9.4%)
Bile fluid culture	2 (3.8%)
Ascitic fluid culture	3 (5.7%)
Pleural fluid culture	3 (5.7%)
Drain fluid culture	12 (22.6%)

Table 4. Microorganisms isolated in pancreatic and extrapancreatic infections in 51 patients with severe acute pancreatitis.

Site	No of micro-organisms	Organism grown
Intraoperative specimen	8	<i>Escherichia coli</i> (4), <i>Enterococcus faecalis</i> (1), <i>Pseudomonas aeruginosa</i> (2), <i>Klebsiella pneumoniae</i> (1)
US/CT aspirate	14	<i>Escherichia coli</i> (8), <i>Enterococcus faecalis</i> (1), <i>Pseudomonas aeruginosa</i> (1), <i>Klebsiella pneumoniae</i> (1), <i>Staphylococcus aureus</i> (2), <i>Acinetobacter baumannii</i> (1)
Blood	21	<i>Staphylococcus aureus</i> (6), <i>Escherichia coli</i> (4), <i>Enterobacter aerogenes</i> (3), <i>Alcaligenes xylosoxidans</i> (2), <i>Enterococcus faecalis</i> (2), <i>Pseudomonas aeruginosa</i> (2), <i>Acinetobacter baumannii</i> (1), <i>Klebsiella pneumoniae</i> (1)
Intravenous site	5	<i>Enterococcus faecalis</i> (1), <i>Klebsiella pneumoniae</i> (1), <i>Staphylococcus aureus</i> (2), <i>Acinetobacter baumannii</i> (1)
Urine	7	<i>Escherichia coli</i> (3), <i>Enterococcus faecalis</i> (1), <i>Yeast</i> (3) ^a
Tracheal aspirate	5	<i>Acinetobacter baumannii</i> (3), <i>Morganella morganii</i> (1), <i>Enterococcus faecalis</i> (1)
NBD fluid	3	<i>Escherichia coli</i> (1), <i>Enterococcus faecalis</i> (1), <i>Pseudomonas aeruginosa</i> (1)
Ascitic fluid	3	<i>Acinetobacter baumannii</i> (1), <i>Enterococcus faecalis</i> (2)
Pleural fluid	3	<i>Acinetobacter baumannii</i> (2), <i>Escherichia coli</i> (1)
Drain fluid	12	<i>Escherichia coli</i> (3), <i>Acinetobacter baumannii</i> (1), <i>Alcaligenes xylosoxidans</i> (1), <i>Staphylococcus aureus</i> (1), <i>Enterococcus faecalis</i> (1), <i>Pseudomonas aeruginosa</i> (1), <i>Proteus mirabilis</i> (1), <i>Yeast</i> (3) ^a

^a Yeast was not taken into consideration in the list of microorganisms in Tables 2 and 5 in which only bacteria were listed.

Since some of the infections were polymicrobial, the total type of organisms are more than the number of infected sites.

CT : computed tomography; NBD: nasobiliary drain; US : ultrasound

(40.9%) of these 22 patients, percutaneous drainage had already been carried out. Surgery was performed on them due to further deterioration despite drainage. In the rest of the patients (n=13; 59.1%), the clinical decision for surgery was taken as per the indications specified in the “Material and Methods” section.

A total of 29 patients died (56.9%). Patients with pancreatic infections had a higher mortality rate as compared to patients without pancreatic infections (16/19, 84.2% vs. 13/32, 40.6%, P=0.003). Mortality was higher in patients with extrapancreatic infections as compared to patients without extra-pancreatic infections (22/32, 68.8% vs. 7/19, 36.8%; P=0.041). Of the 29 patients who died 16 (55.2%) had undergone surgery, while, of the 22 patients who survived, only 6

(27.3%) had undergone surgery. The mortality rate was higher in patients who underwent surgery (59.1% vs. 44.8%) but did not reach statistical significance (P=0.086).

DISCUSSION

In the present study, we investigated pancreatic and extrapancreatic infections in patients with severe acute pancreatitis. Pancreatic infections were observed in 19 (37.3%) patients, with *Escherichia coli* being the most common organism. There was a change in the spectrum of organisms as the pancreatitis progresses, which changed from predominantly gram-negative to gram-positive organisms. Extrapancreatic infections were seen in 32 (62.7%) patients and were more often

Table 5. Antibiotic sensitivity pattern of the pathogens cultured.

Organism	Antibiotic sensitivity
<i>Escherichia coli</i> (n=24)	Amikacin (17; 70.8%), Imipenem (8; 33.3%), Piperacillin+tazobactam (7; 29.2%), Netilmicin (4; 16.7%), Gentamicin (3; 12.5%), Cefoperazone (2; 8.3%), Cefoperazone + sulbactam (2; 8.3%), Chloramphenicol (2; 8.3%), Cefotaxime (1; 4.2%), Nitrofurantoin (1; 4.2%), Ciprofloxacin (1; 4.2%)
<i>Staphylococcus aureus</i> (n=11)	Amikacin (4; 36.4%), Netilmicin (3; 27.3%), Ciprofloxacin (3; 27.3%), Methicillin (3; 27.3%), Rifampicin (3; 27.3%), Vancomycin (2; 18.2%), Cefotaxime (2; 18.2%), Clindamycin (2; 18.2%), Gentamicin (2; 18.2%), Lincomycin (1; 9.1%), Tetracycline (1; 9.1%)
<i>Enterococcus faecalis</i> (n=11)	Vancomycin (5; 45.5%), Piperacillin+tazobactam (3; 27.3%), Penicillin (1; 9.1%), Amoxicillin (3; 27.3%), Nitrofurantoin (1; 9.1%), Erythromycin (1; 9.1%)
<i>Acinetobacter baumannii</i> (n=10)	Cefoperazone + sulbactam (5; 50.0%), Imipenem (4; 40.0%), Piperacillin+tazobactam (4; 40.0%), Amikacin (3; 30.0%), Gentamicin (3; 30.0%), Netilmicin (2; 20.0%), Ofloxacin (1; 10.0%), Tetracycline (1; 10.0%), Cefotaxime (1; 10.0%), Ceftazidime (1; 10.0%), Nitrofurantoin (1; 10.0%)
<i>Pseudomonas aeruginosa</i> (n=7)	Imipenem (4; 57.1%), Amikacin (4; 57.1%), Piperacillin+tazobactam (3; 42.9%), Netilmicin (2; 28.6%), Gentamicin (1; 14.3%), Chloramphenicol (1; 14.3%)
<i>Klebsiella pneumoniae</i> (n=4)	Imipenem (3; 75.0%), Piperacillin+tazobactam (2; 50.0%), Ciprofloxacin (2; 50.0%), Cefotaxime (1; 25.0%), Ceftazidime (1; 25.0%)
<i>Enterobacter aerogenes</i> (n=3)	Piperacillin+tazobactam (2; 66.7%), Netilmicin (1; 33.3%), Cefoperazone + sulbactam (1; 33.3%), Imipenem (1; 33.3%), Amikacin (1; 33.3%)
<i>Alcaligenes xylosoxidans</i> (n=3)	Cotrimoxazole (2; 66.7%), Ciprofloxacin (1; 33.3%), Gentamicin (1; 33.3%), Netilmicin (1; 33.3%), Amikacin (1; 33.3%)
<i>Morganella morganii</i> (n=1)	Imipenem (1; 100%), Amikacin (1; 100%)
<i>Proteus mirabilis</i> (n=1)	Imipenem (1; 100%)

polymicrobial as compared to pancreatic infections (53.1% vs. 26.3%; $P=0.083$). We have studied the characteristics and impact of pancreatic and extrapancreatic infections on the clinical course of these patients separately.

In accordance with the reports of other studies [15, 16], the prevalence of the pancreatic infections correlated with the extent of the necrosis. There was a shift from gram-negative to gram-positive organisms with increase in length of hospital stay. The most common mechanism involved in the pathogenesis of the pancreatic infections was the translocation of bacteria from the gut [17, 18]. This could explain pancreatic infection with *Escherichia coli*, which is reported to be the most common organism in this setting [19]. Subsequent infection with gram-positive organisms could be secondary to nosocomial blood stream invasion. In patients with pancreatic infections, monomicrobial infections were more common than polymicrobial infections. Similar findings have been reported in other studies in the literature [19]. Polymicrobial infections are more common in patients with pancreatic abscess as compared to patients with infected pancreatic necrosis [20]. Most of the other studies in the literature have also found *Escherichia coli* to be the most common isolate [2, 19, 21]. However, Gerzof *et al.* [3] reported *Klebsiella* to be the most common isolate.

Extrapancreatic infections have not been the focus of attention of many studies. We had 53 positive cultures in 32 patients with 19 cultures being positive in the first week, 9 in the second week and 25 in the third week and later. There was no correlation between the occurrence of pancreatic and extrapancreatic infections or the organisms grown at the two sites. The most common extrapancreatic site involved was the blood stream with positivity documented in 16 (30.2%) cultures followed by drain fluid culture positivity in 12 (23.5%) patients. While *Escherichia coli* was the most common organism in urine and drain fluid, *Staphylococcus aureus* was the most common organism in the blood and *Acinetobacter baumannii* in the tracheal aspirate.

The timing and correlation of extrapancreatic infections with pancreatic infections in patients with acute pancreatitis has previously been investigated only in a few studies. In an animal model of acute pancreatitis involving 65 rats, extrapancreatic bacterial infections were investigated in the spleen, liver, mesenteric lymph nodes, peritoneal cavity and blood. The animals were sacrificed at 8, 16, 24 and 32 hours after the induction of acute pancreatitis. The peak of bacterial culture positivity was seen at 16-24 hours in the spleen and liver. There was no bacterial growth in the mesenteric lymph nodes in the 8-hour group. However, after 16, 24, and 32 hours, 46.2%, 76.9%, and 38.5% of the cultures were positive, respectively. Bacteria could be cultured from the peritoneal cavity in 53.9% of the control group and in 76.9 to 92.3% of the animals with pancreatitis [9]. In a study of 212 patients

with acute pancreatitis, Bourgaux *et al.* [22] reported extrapancreatic infections in 25% of their patients. The most common sites of infection were the peritoneal fluid (26.8%), blood (24.4%), respiratory tract (24.4%) and urinary tract (19.5%). Infections were polymicrobial in 37.5% of patients. The median time between the onset of the pancreatitis and the diagnosis of the infection was 4 days; it was shorter than that of pancreatic infections.

In a study by Garg *et al.* [19], extrapancreatic bacterial infections were found in 31.7% of the 63 patients. Acute cholangitis occurred in 6 patients, intravenous site infection in 5 patients, and urine and peritoneal fluid infection occurred in 3 patients each. The most common organisms isolated were *Escherichia coli* in 25% of the cultures and *Pseudomonas aeruginosa* in 23% of the cultures. In a recent study by Besselink *et al.* [23], bacteremia was reported in 13.4% and pneumonia in 11.5% of patients with their first episode of acute pancreatitis. Bacteremia and pneumonia were diagnosed earlier than infected necrosis. They found gram-negative bacteria to be the most common isolates. However, a tendency towards an increase in gram-positive bacteria has been noted in several series [1, 10, 24]. This might be explained by the use of prophylactic antibiotic therapy against gram-negative bacteria [10].

Differences in the types of microorganisms between pancreatic and extrapancreatic infections may reflect the different sources of infection. While the predominant gram-negative bacteria in pancreatic infections are derived from the endogenous bowel microflora [25], the source of predominant gram-positive bacteria in extrapancreatic infections is probably exogenous nosocomial. Factors which predispose these patients to infections include the use of intravascular, percutaneous and urinary catheters, mechanical ventilation and surgical intervention. Willdison *et al.* [26] showed a higher incidence of bacteremia in patients with pancreatic infections. The source of bacteremia was respiratory (17%), genitourinary (17%), biliary (3%), skin (3%) and the intravenous site (3%).

The presence of pancreatic infections adversely affected the outcome of these patients with mortality being significantly higher in patients with pancreatic infections. Surgical intervention was another factor which adversely affected the outcome of these patients with mortality being significantly higher in patients who underwent surgery. We also found higher mortality rates in patients with extrapancreatic infections. In another study [23], patients with infected pancreatic necrosis had a 2.5 times higher mortality rate if bacteremia or pneumonia was documented. Bacteremia is a risk factor for infection of pancreatic necrosis; the cultured pathogens point to the gut as the source of the pathogen [23]. The presence of bacteremia should raise the level of suspicion for infected necrosis in a patient already diagnosed with pancreatic necrosis.

The antibiotic sensitivity pattern of our patients showed that most of the organisms were sensitive to beta lactum antibiotics, aminoglycosides and imipenem. In a study of incidence, spectrum and antibiotic sensitivity pattern of bacterial infections among patients with acute pancreatitis, Garg *et al.* [19] noted that most bacterial isolates were sensitive to third generation cephalosporins and quinolones. Imipenem, cephalosporins and quinolones are the antibiotics which achieve high pancreatic tissue concentration [27, 28, 29, 30].

Our study has a few limitations. We have not studied anaerobic infections, although they have occasionally been found in patients with severe acute pancreatitis [3, 22]. Our study included only patients with severe acute pancreatitis; bacterial infections in patients with milder grades of pancreatitis were therefore not studied. Most of our patients were referred; they had already received treatment at primary and secondary level hospitals, details of which could not be ascertained. We have not classified the infections into primary and secondary because many of the patients had already undergone interventions in other institutions before admission to our centre.

In conclusion, we observed pancreatic infections in 37.3% of patients and extrapancreatic infections in 62.7% of patients with severe acute pancreatitis. The pancreatic infections were most often monomicrobial while the extrapancreatic infections were more often polymicrobial. In patients with pancreatic infection, there was a change in the spectrum of the microorganisms from gram-negative to gram-positive with increase in the progression of the disease. The most common site of the extrapancreatic infections was blood stream invasion. The present study showed that the presence of pancreatic as well as extrapancreatic infections adversely affected the outcome of patients with severe acute pancreatitis. In addition to pancreatic infections, early detection and treatment of extrapancreatic infections may positively affect patient outcome. The effect of the treatment of extrapancreatic infections on patient outcome should be investigated in future studies. The results of the sensitivity pattern of the microorganisms suggest that cephalosporins and imipenem should be used as the empirical antibiotics of choice in patients with severe acute pancreatitis.

Conflict of interest The authors have no potential conflict of interest

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