International Surgery Journal
Krishna SP et al. Int Surg J. 2021 Dec;8(12):3569-3575
http://www.ijsurgery.com
pISSN2349-3305 | eISSN2349-2902

DOI: https://dx.doi.org/10.18203/2349-2902.isj20214747

Original Research Article

Pancreatic duct fluid culture in patients with chronic pancreatitis undergoing operative intervention and its implications on post operative course

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Received: 31 August 2021
Revised: 14 October 2021
Accepted: 27 October 2021

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ABSTRACT

Background: The role of bacteria in pathogenesis of chronic pancreatitis is poorly understood. Our aim was to analyse pancreatic duct fluid culture in patients undergoing operative intervention for chronic pancreatitis and its implications in post operative outcomes.
Methods: Among 35 patients, 17 underwent Freys, 13 underwent longitudinal pancreatico-jejunostomy, 5 underwent cystojejunostomy. Duct fluid culture was obtained intraoperatively and analysed and compared with preoperative parameters and post operative outcomes.
Results: 20 patients had positive duct fluid culture. Most common pathogen isolated was Klebsiella (8 patients). The only preoperative parameter which showed significant association was fasting blood glucose level. Wound infections were seen in 11 of which 10 had positive duct culture, out of which 9 had the same organism of that in duct culture. Mean hospital stay was 9±1.07 and 10±1.13 days in patients without and with infectious complications respectively.
Conclusions: Older concept of sterile PD fluid in patients with CP may no longer hold true. In our study upto 60% of patients showed positive PD culture. By starting appropriate antibiotic we can reduce the length of hospital stay in patients who have septic complications. However large centre studies may guide us further into the importance of this concept and the role of bacteria in the pathogenesis of CP.

Keywords: Chronic pancreatitis, Pancreatic duct, Culture, Wound infection

INTRODUCTION

Chronic pancreatitis is fibroinflammatory disease of the exocrine pancreas where recurrent episodes of pancreatic inflammation of variable intensity and duration leads to irreversible pancreatic tissue damage.[1,2] Although several causes have been described in the literature in which some differ in their natural history, most patients will develop typical clinical and morphological features which includes parenchymal or intraductal calcifications, pancreatic fibrosis, exocrine and endocrine pancreatic insufficiency. Without prior percutaneous and endoscopic intervention, pancreatic duct fluid is considered to be sterile in patients suffering from CP.[3]

A study in the past showed presence of bacteria in PD fluid in almost 64% of patients with CP who had no prior history of interventions.[4]Thesignificance of such positive PD fluid cultures is not well established. We propose a study to analyse prospectively the bacteriological profile and antibiotic sensitivity for patients with CP who have positive PD fluid culture and its association with postoperative outcome.

METHODS

We conducted this prospective study from October 2016 to March 2021 in a GI surgical unit from a tertiary referral hospital, government Mohan Kumaramangalam government hospital, Salem. 35 patients were included in the study where 22 (62.9%) were males and 13 (37.1%) were females. Patients who had suspicion of CP were admitted and diagnosis was confirmed by trans-abdominal ultrasound screening, followed by contrast enhanced computed tomography of the abdomen and pelvis. According to patient symptomology upper GI endoscopy and MRCP were done as additional investigations. Patients age, gender, aetiology, clinical presentation, CECT findings, preoperative workup, intraoperative findings, choice of surgical intervention and postoperative events were registered prospectively into the database.

Inclusion criteria

Patients had to meet the following inclusion criteria; patients diagnosed on CECT abdomen with CP with any one indication for surgery in terms of intractable pain, inflammatory head mass (defined as diameter of 35 mm in contrast enhanced computed tomography), with bile duct obstruction or duodenal obstruction or other adjacent organ complications were included.

Exclusion criteria

The exclusion criteria for this study were; any contraindication for surgical management in view of severe and uncontrolled comorbidity and/or patient unfit for long operative procedure under general anaesthesia. Signs of localized or generalized infection. Prior antibiotic treatment within the last 2 weeks of presentation. Treatment with corticosteroids or any other immunosuppressive drugs. Patients who had prior intervention in the form of endoscopic cannulation or stenting of pancreatic duct for chronic pancreatitis.

Procedure

On the basis of intraoperative findings, patients underwent either Frey's procedure, Roux-en-Y cysto jejunostomy or Roux-en-Y lateral pancreatico-jejunostomy. A minimum of 1ml of PD fluid was obtained before laying it open using a 22G needle taking care to avoid contamination with blood. In case of pseudocyst fluid is obtained from the cyst. The aspirates were sent for microbiological analysis. Subsequently biochemical analysis of the organism and antibiotic sensitivity patterns were noted. When colonies were noted on agar surface, a gram staining was done and subsequently subcultures were done on aerobic and Brewer's anaerobic agar plates. The post operative complications were noted which included surgical site infections (superficial, deep and organ space infection), anastomotic leak and mortality. Patients who had the above complications in our study were subjected to wound, blood and drain fluid cultures and antibiotic sensitivity was tested.

Statistical analysis

Data were coded and recorded in MS Excel spreadsheet program. SPSS v23 (IBM Corp.) was used for data analysis. Descriptive statistics were elaborated in the form of means/standard deviations and medians/IQRs for continuous variables, and frequencies and percentages for categorical variables. Data were presented in a graphical manner wherever appropriate for data visualization using histograms/Box-and-Whisker plots/column charts for continuous data and bar charts/pie charts for categorical data. Group comparisons for continuously distributed data were made using independent sample 't' test when comparing two groups. If data were found to be non-normally distributed, appropriate non-parametric tests in the form of Wilcoxon test were used. Chi-square test was used for group comparisons for categorical data. In case the expected frequency in the contingency tables was found to be <5 for >25% of the cells, Fisher's Exact test was used instead. Linear correlation between two continuous variables was explored using Pearson's correlation (if the data were normally distributed) and Spearman's correlation (for non-normally distributed data). Statistical significance was kept at $p<0.05$.

RESULTS

Patient cohort

Thirty five patients with CP who underwent operative intervention were included in our study. The median age was 45.17±12.49 years and the most common age group being from 41to50 years (42.9%). Most common aetiology was alcohol (60%). Out of the 35 patients, 16 (45.71%) had diabetes mellitus and blood glucose was well under control before they were subjected to surgery. The mean total leucocyte count (pre-operative) was 8399.89±1020.74 cells/cumm. The mean albumin (pre-operative) was 3.52±0.62 gm/dl.

Pancreatic parameters and operative interventions

Thirty one patients had pancreatic calcifications. 5 of which had pseudocyst arising from body of pancreas. 17 (54.8%) of the patients underwent Freys procedure. 13 (37.1%) patients underwent longitudinal pancreatico-jejunostomy. 5 (14.3%) patients had pseudocyst arising from the body of pancreas and underwent Roux-en-Y cystojejunostomy. Summary of baseline patient details is given in (Table 1).

Bacteriological profile

Twenty (57.1%) of the patients had positive PD fluid culture. *Klebsiella pneumonia* was the most common organism isolated in about 8 patients (22.9%) followed by Escherichia coli which was seen in 6 patients (17.1%). A small minority of patients had *Pseudomonas aeruginosa* in 4 cases (11.4%) and *Streptococcus pneumonia* which was seen in 2 cases (5.7%). Distribution of organism in PD fluid culture is depicted in (Figure 1).

Table 1: Patient baseline parameters.

Basic Details	Observation
Age (years), mean ±SD, median (IQR), range	45.17 ± 12.49, 45.00 (39.50-50.00), 16.00 - 75.00
Age (years), frequency (%)	
≤20	2 (5.7)
21-30	1 (2.9)
31-40	9 (25.7)
41-50	15 (42.9)
51-60	4 (11.4)
61-70	3 (8.6)
71-80	1 (2.9)
Gender	
Male	22 (62.9)
Female	13 (37.1)
TLC (pre-operative), mean ±SD, median (IQR), range	8399.89±1020.74, 8571.00 (7653.00-9271.50), 6208.00-10084.00
Blood sugar (pre-operative), mean ±SD, median (IQR), range	101.31±17.18, 102.00 (86.00-113.50), 72.00-134.00
Albumin (pre-operative), mean ±SD, median (IQR), range	3.52 ± 0.62, 3.60 (2.95-4.00), 2.40-4.60
MPD diameter (mm), mean ±SD, median (IQR), range	7.42 ±1.93, 6.80 (6.10-8.85), 4.20 - 11.40
MPD diameter (mm), frequency (%)	
<7	18 (51.4)
≥7	17 (48.6)
Procedure done, frequency (%)	
Freys Procedure	17 (54.8)
LPJ	13 (37.1)
Cystojejunostomy	5 (14.3)

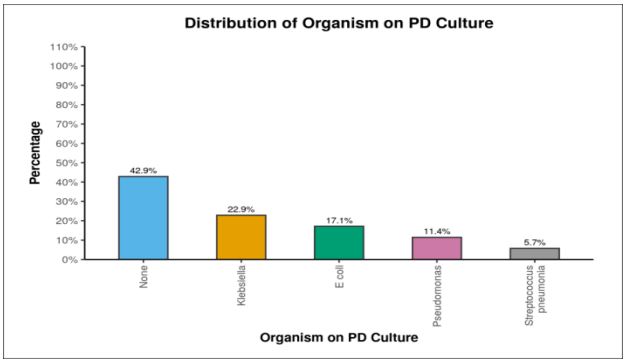

Figure 1: Distribution of organism in MPD culture.

Post operative outcomes

Superficial surgical site infections were seen in 11 patients out of which 10 patients had positive PD fluid culture. Most common wound cultures were *Escherichia coli* seen in 5 patients followed by 4 who had positive *Klebsiella pneumonia*. *Pseudomonas aeruginosa* as positive wound culture was seen 2 patients. One patient who had *Klebsiella pneumonia* isolated in PD fluid had positive wound cultures for *Escherichia coli*.

We had one mortality in our study who underwent Freys. He had positive PD fluid cultures for *Klebsiella pneumonia* and subsequent positive cultures for the same organism in wound drain fluid and blood. Patient preoperatively had chronic kidney disease and diabetes mellitus. He was on regular dialysis and his preoperative creatinine clearance was 82 ml/min. After the intervention patient had sepsis induced acute kidney and lung injury, who eventually succumbed. Mean length of hospital stay was 9±1.07 days in patients without infectious complications and 10±1.13 days in those with septic complications. Summary of various cultures is given in (Table 2, Figure 2). Summary of bacteriological profile is given in (Table 3, Figure 3).

Table 2: Summary of various cultures.

Culture	Positive N (%)	Negative N (%)
PD Culture	20 (57.1)	15 (42.9)
Blood Culture	2 (5.7)	33 (94.3)
Wound Culture	11 (31.4)	24 (68.6)
DT Culture	5 (14.3)	30 (85.7)

Table 3: Bacteriological profile of various cultures.

Organism	None	*E coli*	*Klebsiella*	*Pseudomonas*	*Streptococcus pneumonia*
Organism on PD culture	15 (42.9)	6 (17.1)	8 (22.9)	4 (11.4)	2 (5.7)
Organism on blood culture	33 (94.3)	0 (0.0)	1 (2.9)	1 (2.9)	0 (0.0)
Organism on wound culture	24 (68.6)	5 (14.3)	4 (11.4)	2 (5.7)	0 (0.0)
Organism on DT culture	30 (85.7)	2 (5.7)	2 (5.7)	1 (2.9)	0 (0.0)

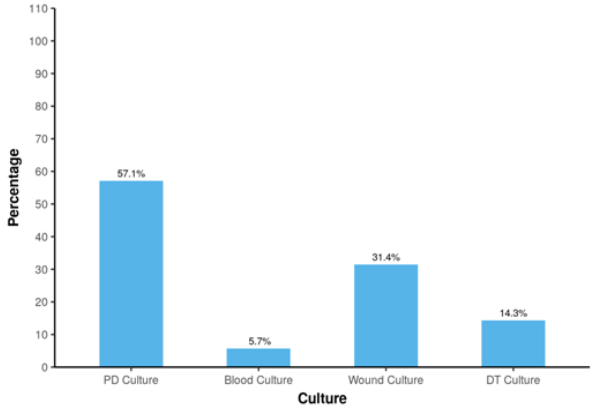

Figure 2: Summary of various cultures.

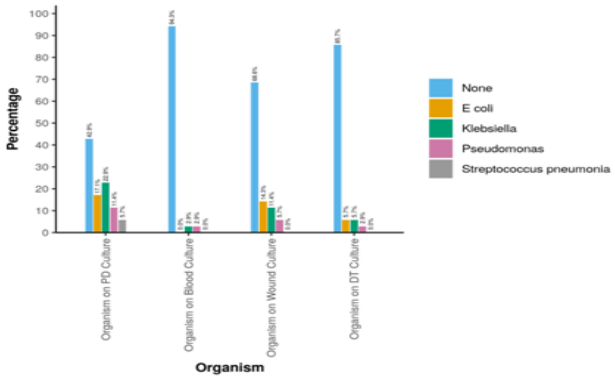

Figure 3: Bacteriological profile of various cultures.

DISCUSSION

In the past 60 years several hypothesis were postulated to explain the pathogenesis of CP but none have explained the pathogenic process clearly.[5] Sah et al gave six major established theories for pathogenesis which included necrosis-fibrosis, protein plug, oxidative stress, toxic metabolite, primary duct hypothesis and SAPE.[6] Association of bacteria or virus in the pathogenesis of CP is unclear as opposed to the same in biliary system where microbial products have recently been proposed as potential triggers for biliary diseases.[7] The relationship between *helicobacter pylori* and CP, and in particular autoimmune CP has been the subject of interest in the recent years.[8] It has been suggested previously that H. pylori infection exists as a possible common cause of these conditions acting *via* a mechanism involving the molecular mimicry of host structures.[9] However, till date no such association is established between H. Pylori and chronic or autoimmune pancreatitis.[10]

Although the PD fluid culture in patients suffering from CP is thought to be sterile, especially in whom no prior intervention was done, J. A Gregg in 1977 showed positive PD fluid cultures in 11 of 35 patients with pancreatitis and 3 of 5 with pancreatic cancer. The pancreatic juice was sterile in 25 controls. Cultures from the common bile duct in 9 controls were also sterile whereas 4 of 6 with pancreatitis showed infected bile. The infecting organisms were principally gram-negative, and the infections were usually polymicrobial. He also noticed that antibiotics, where used, successfully eradicated the infecting organisms but did not appear to affect the patient's clinical course.[11] In our study of 35 patients with CP, 20 (57.1%) of the patients had positive PD fluid culture in whom *Klebsiella pneumonia* was the most common pathogen isolated in about 8 patients (22.9%). *Escherichia coli* was isolated in 6 patients (17.1%) followed by *Pseudomonas aeruginosa* in 4 cases (11.4%) and *Streptococcus pneumonia* which was seen in 2 cases (5.7%). Similarly Yallamali et al in 2011 showed positive PD fluid cultures in 64% of patients who had CP without prior intervention. *Escherichia coli* followed by *Pseudomonas aeruginosa* were the most frequent organisms.[4]

Table 4: Comparison of the 2 subgroups of the variable PD culture in terms of fasting blood Sugar (pre-operative).

Blood sugar (pre-operative)	PD culture		t test	
	Positive	**Negative**	**t**	**P value**
Mean (SD)	107.60 (17.11)	92.93 (13.71)	2.814	0.008
Median (IQR)	110.5 (96.5-119.5)	91 (82-104.5)		
Range	72 - 134	73 - 115		

Table 5: Comparison of PD culture with various variables.

Parameters	PD Culture		P value
	Positive (N=20)	Negative (N=15)	
Age (years)	45.40±10.91	44.87±14.73	0.907
Age (years)			0.514
≤20	1 (5.0)	1 (6.7)	
21-30	0 (0.0)	1 (6.7)	
31-40	4 (20.0)	5 (33.3)	
41-50	11 (55.0)	4 (26.7)	
51-60	2 (10.0)	2 (13.3)	
61-70	2 (10.0)	1 (6.7)	
71-80	0 (0.0)	1 (6.7)	
Gender			0.686
Male	12 (60.0)	10 (66.7)	
Female	8 (40.0)	5 (33.3)	
TLC (Pre-Operative)	8438.05 ± 874.08	8349.00 ± 1220.08	0.812
Blood Sugar (Pre-Operative)	107.60 ± 17.11	92.93 ± 13.71	0.008
Albumin (Pre-Operative)	3.50 ± 0.63	3.55 ± 0.62	0.787
MPD Diameter (mm)	7.66 ± 2.11	7.10 ± 1.69	0.341
MPD Diameter (mm)			0.118
<7	8 (40.0)	10 (66.7)	
≥7	12 (60.0)	5 (33.3)	
Blood Culture (Positive)	2 (10.0)	0 (0.0)	0.496
Wound Culture (Positive)	9 (45.0)	2 (13.3)	0.069
DT Culture (Positive)	5 (25.0)	0 (0.0)	0.057
Organism on PD Culture* **			<0.001
None	0 (0.0)	15 (100.0)	
Klebsiella	8 (40.0)	0 (0.0)	
E coli	6 (30.0)	0 (0.0)	
Pseudomonas	4 (20.0)	0 (0.0)	
Streptococcus pneumonia	2 (10.0)	0 (0.0)	
	Positive (N=20)	**Negative (N=15)**	
Organism on blood culture			1.000
None	18 (90.0)	15 (100.0)	
Klebsiella	1 (5.0)	0 (0.0)	
Pseudomonas	1 (5.0)	0 (0.0)	
Organism on wound culture			0.289
None	11 (55.0)	13 (86.7)	
E coli	4 (20.0)	1 (6.7)	
Klebsiella	3 (15.0)	1 (6.7)	
Pseudomonas	2 (10.0)	0 (0.0)	
Organism on DT culture			0.313
None	15 (75.0)	15 (100.0)	
E coli	2 (10.0)	0 (0.0)	
Klebsiella	2 (10.0)	0 (0.0)	
Pseudomonas	1 (5.0)	0 (0.0)	

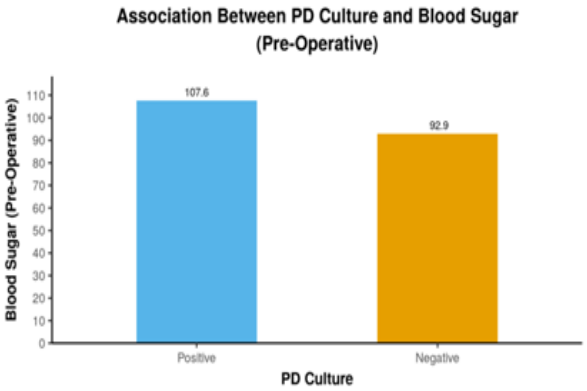

Figure 4: Comparison of the 2 subgroups of the variable PD culture in terms of fasting blood Sugar (pre-operative).

In a recent study by Salil et al in 2014, PD fluid culture was positive for bacteria in 11 (42%) patients. Wound infection was seen in 11 patients. *Escherichia coli* was the commonly isolated organism, seen in 5 patients. Escherichia coli was a common pathogen in both wound and PD fluid culture in 2 patients, showing a microbiological role in wound infection.[3] Similarly in our study superficial surgical site infections were seen in 11 patients, out of which 10 had positive PD fluid culture. Of this 10, 9 had the same organism isolated showing a significant association.

Moreover 5 patients had the same organism in drain fluid, further showing supportive evidence. Sensitivity pattern was noted and appropriate antibiotics were given. 9 patients with superficial surgical site infection responded well. Such association for specific antibiotic therapy based on intraoperative culture is well established for biliary tract diseases.[12,13] The mean length of hospital stay was 9±1.07 days in patients without infectious complications and 10± 1.13 in patients with infectious complications which is comparable. This is probably due to the administration of appropriate antibiotics based on PD fluid culture and sensitivity.

The only preoperative patient parameter which showed significant association was preoperative fasting blood glucose level. The mean (SD) of fasting blood sugar (pre-operative) in the PD fluid culture positive group was 107.60 (17.11). The mean (SD) of fasting blood Sugar (pre-operative) in the PD fluid culture negative group was 92.93 (13.71).The association is significant (t=2.814, p=0.008). Though these blood sugar levels have no clinical relevance. Comparison of the 2 subgroups of the variable pancreatic duct culture in terms of fasting blood sugar (pre-operative) is depicted in (Table 4, Figure 4). Comparison of pancreatic duct culture with variables is depicted in (Figure 9).

CONCLUSION

Older concept of sterile PD fluid in patients with CP may no longer hold true. In our study upto 60% of patients showed positive PD culture. By starting appropriate antibiotic we can reduce the length of hospital stay in patients who have septic complications. However large centre studies may guide us further into the importance of this concept and the role of bacteria in the pathogenesis of CP.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Hoffmeister A, Mayerle J, Beglinger C. English language version of the S3-consensus guidelines on chronic pancreatitis: Definition, aetiology, diagnostic examinations, medical, endoscopic and surgical management of chronic pancreatitis. Z Gastroenterol. 2015;53(12):1447-95.
2. Kleeff J, Whitcomb DC, Shimosegawa T. Chronic pancreatitis. Nat Rev Dis Primers. 2017;3:17060.
3. Parida SK, Pottakkat B, Raja K, Vijayahari R, Lakshmi CP. Bacteriological profile of pancreatic juice in patients with chronic pancreatitis. JOP. 2014; 15(5):475-7.
4. Yelamali A, Mansard M, Rao P, Dama R, Rebela P, Rao GV, Reddy N. Bacteriology of pancreatic fluid in chronic calcific pancreatitis. J Gastroenterol Hepatol. 2011;26 (5): 23.
5. Brock C, Nielsen LM, Lelic D, Drewes AM. Pathophysiology of chronic pancreatitis. World J Gastroenterol. 2013;19(42):7231-40.
6. Sah RP, Dawra RK, Saluja AK. New insights into the pathogenesis of pancreatitis. Curr Opin Gastroenterol. 2013;29(5):523-30.
7. Verdier J, Luedde T, Sellge G. Biliary Mucosal Barrier and Microbiome. Viszeralmedizin. 2015; 31(3):156-61.
8. Kim KP, Kim MH, Song MH, Lee SS, Seo DW, Lee SK. Autoimmune chronic pancreatitis. Am J Gastroenterol. 2004;99(8):1605-16.
9. Kountouras J, Zavos C, Chatzopoulos D. A concept on the role of Helicobacter pylori infection in autoimmune pancreatitis. J Cell Mol Med. 2005;9(1): 196-207.
10. Jesnowski R, Isaksson B, Möhrcke C, Bertsch C, Bulajic M, Schneider-Brachert W et al Helicobacter pylori in autoimmune pancreatitis and pancreatic carcinoma. Pancreatology. 2010;10(4):462-6.
11. Gregg JA. Detection of bacterial infection of the pancreatic ducts in patients with pancreatitis and pancreatic cancer during endoscopic cannulation of the pancreatic duct. Gastroenterology. 1977;73(5): 1005-7.

12. Rubén CR, Marco HG, Edelmiro PR, Francisco RS, Gerardo MM. Incidence of bacteria from cultures of bile and gallbladder wall of laparoscopic cholecystectomy patients in the University Hospital. Eleuterio González. 2017;85(6):515-21.
13. Chandra S, Klair JS, Soota K, Livorsi DJ, Johlin FC. Endoscopic Retrograde Cholangio-Pancreatography-Obtained Bile Culture Can Guide Antibiotic Therapy in Acute Cholangitis. Dig Dis. 2019;37(2):155-60.

Cite this article as: Krishna SP, Somasekar RDR, Sivasankar A, Kesavan B, Chidambaram PM, Ramamurthy C. Pancreatic duct fluid culture in patients with chronic pancreatitis undergoing operative intervention and its implications on post operative course . Int Surg J2021;8:3569-75.