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The Infectious Complications of Biliary Decompression Prior to Pancreaticoduodenectomy in a Patient with Obstructive Jaundice

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Abstract **Original Research Article**

Background: The standard of therapy for benign diseases, periampullary and ampullary cancers is pancreaticoduodenectomy (PD). These patient subgroups frequently present with obstructive jaundice, which is associated with increased morbidity due to impaired immunity and nutrition. It is controversial whether PBD should be applied routinely prior to pancreaticoduodenectomy. **Objective:** The purpose of this study is to investigate infectious complications of biliary decompression prior to pancreaticoduodenectomy in a patient with obstructive jaundice. ***Methods:*** This single-center, cross-sectional study was done at BSMMU from April 2021 to March 2022. The study comprised 48 pancreaticoduodenectomy patients who met the criteria. Two groups formed. Group I had preoperative biliary drainage (n=24) while Group II did not (n=24). After written consent, all patient data was collected in a standardized form. SPSS version 23.0 ran statistical analysis. Unpaired t-test was used to evaluate mean SD quantitative variables. Chi-square test was conducted to see any association between qualitative observations and frequencies and percentages. P 0.05 was considered statistically significant in 95% confidence interval tests. ***Results:*** Overall infectious complications were not significant between two group (75%vs 41.7%; p=0.097). But SSI was higher in stent group (p=0.040). This stent group also observed higher positive bile culture 83.3% with significant polymicrobial growth (p=0.012). Commonly used antibiotics showed higher resistance to those biliary organisms; Cephalosporin (50 75%), Carbapenem (41.7%). There was also significant association between positive bile culture with SSI (p=0.048). Per- operative adhesion (p=0.001) and blood loss (p= 0.006) observed more in stent group. Although significant improvement of liver function observed following stenting. ***Conclusions:*** Increased risk of resistant polymicrobial bactibilia with strong association with SSI; preoperative biliary stenting in patients undergoing PD should be used only in selected patients.

Keywords: Wound Infection, Pancreaticoduodenectomy, Stent, Pre-operative biliary drainage.

INTRODUCTION

In patients with both benign and malignant diseases, obstruction of the distal common bile duct is the most common presenting symptom, manifesting as jaundice. Hepatic malfunction, coagulation disorder, cholangitis, compromised cellular immunity, and renal failure are all well-documented negative outcomes of obstructive jaundice. This means that patients with these conditions may have a higher risk of problems during surgery, especially during a more involved operation like a pancreaticoduodenectomy (PD) [1, 2].

Preoperative biliary drainage (PBD) has thus been practiced at several hospitals for many years. Reduced postoperative complications were hoped to result from the use of PBD in these patients by lowering their serum bilirubin levels. According to the available

data, biliary drainage has the potential to boost immunity, enhance nutritional status, and lessen susceptibility to infection. The goal was to improve biliary outflow and thereby return the body to a normal physiological state [3, 2]. Surgery can be scheduled at a later time in a high-volume hospital if preoperative biliary drainage is performed at a less specialized center without the ability to undertake urgent pancreatic surgery. In addition to making patients candidates for neoadjuvant therapy, preoperative biliary stenting improves patient outcomes. So, some researchers advocate for the usage of PBD due to its benefits in reducing postoperative problems [3-5].

However, biliary stenting disturbs the mechanical barrier function of the oddi's sphincter and predisposes to ascending infection from the duodenum, and so, endoscopic and / or percutaneous biliary drainage may increase the risk of bacterial colonization of the bile. Infectious issues after surgery are already common, but bile colonization has been linked to an even higher rate of infection.

Surgery-related Deaths and Illnesses [1, 5, 6]. Additionally, a meta-analysis found that biliary drainage prior to surgery significantly improved (P.001), rather than reducing them, and offered no benefit in terms of reduced mortality or shorter hospital stay [6, 7]. Stent patients, in particular those who have undergone pancreaticoduodenectomy, have been linked by some writers to a significantly higher frequency of post-operative wound infections [1, 8].

Biliary decompression provides symptomatic relief to patients with pruritus and cholangitis, or can serve as a temporizing measure if surgery is delayed or neoadjuvant therapy is considered. However, an opposing body of evidence reports worse outcomes in patients that undergo preoperative biliary decompression. Infectious complications such as wound infection, intraabdominal abscess, bactaraemia and urinary tract infection are higher with biliary decompression. Its routine implementation has become controversial and its diagnostic or therapeutic benefit is no longer clear now. It has been argued that biliary decompression in patients with jaundice before pancreaticoduodenectomy surgery may be beneficial. So considering this dilemma, the aim of this study is set to assess the infectious complications following pancreaticoduodenectomy in patients with obstructive jaundice with pre-operative biliary decompression.

OBJECTIVE

- To assess the infectious complications of biliary decompression prior to pancreaticoduodenectomy in a patient with obstructive jaundice.

METHODS AND MATERIALS

This was a single centered, cross-sectional study conducted in the department of Hepatobiliary pancreatic and liver transplant surgery, BSMMU over a period of one year from April 2021 to March 2022. A total of 48 patients who fulfilled the enrollment criteria & underwent pancreaticoduodenectomy were included in the study. All patients of both gender suffering from malignant obstructive jaundice underwent pancreaticoduodenectomy attended in the Department of Hepatobiliary Pancreatic & Liver Transplant Surgery, BSMMU, Dhaka during the study period were included in the study.

Inclusion Criteria

- All adult patients who will undergo pancreaticoduodenectomy due to malignant obstructive jaundice.

Exclusion Criteria

- Immuno Compromised patients including patients on steroid therapy.
- History of recent failed ERCP.
- History of recent Cholangitis.
- Hepatic or renal insufficiency.
- Not willing to participate.

Data Collection and Analysis

They were divided into two groups. In Group I who had preoperative biliary drainage in other hospital prior to admission (n=24) and in Group II who directly admitted to our department without PBD (n=24). All the data from the patients were collected in a structured data collection sheet after written consent. Statistical analyses were carried out by SPSS version 23.0. Quantitative variables were presented as mean ± standard deviation and analyzed by the Un-paired t-test. The qualitative observations were indicated by frequencies and percentages; Chi-Square test was used to see any association. The statistical tests were conducted with the 95% confidence interval and P <0.05 was considered as statistically significant.

RESULTS

Table 1 shows demography of 48 patients included in the study. The mean age was 51.83±12.46 (range 36-76) years in group I and 52.5±11.58 (range 30-76) years in group II. Male and female participants were 66.7% and 33.3% in group I respectively and 50% & 50% in group II. In group I 66.7% patient came from rural area whereas 33.3% from urban and in group II 41.7% and 58.3% respectively. 50% patients had diabetes mellitus in group I and 41.6% in group II. Hypertension was found in 33.3 percent of group I participants and 25% of group II participants. Diabetes mellitus was found in 50% in group I and 41.6% in group II. Ampullay, Periampullary and Cholangiocarcinoma were 50%, 41.7% and 8.3%

among group I and 25%, 66.7% and 8.3% among group II respectively. No patient with pancreatic malignancy was found during the study period. Therefore, patients of both groups have similar background before operation.

Table 1: Demographics of patients (n=48)

Variables	Group I (n=24)		Group II (n=24)		P Value
Age in years, Mean±SD	51.83±12.46		52.5±11.58		[a]0.892[ns]
Range (min-max)	36-76		30-73		
Gender					
Male	16	66.7	12	50.0	[b]0.407[ns]
Female	8	33.3	12	50.0	
Place of residence					
Rural	16	66.7	10	41.7	[b]0.219[ns]
Urban	8	33.3	14	58.3	
Co-morbidities					
Diabetes	12	50.0	`10	41.6	[b]0.913[ns]
Hypertension	8	33.3	6	25.0	
Indication of surgery					
Ampullary	12	50	6	25	
Periampullary	10	41.7	16	66.7	[b]0.429[ns]
Cholangiocarcinoma	2	8.3	2	8.3	
Pancreatic carcinoma	0	0	0	0	

Table 2 shows the difference of pre-operative liver function between two groups. S. bilirubin level was significantly (p value 0.001) lower in group I (3.25±2.71; range: 0.6- 9.2) mg/dl than group II (9.47±5.13; range: 3.8-19) mg/dl. Serum alkaline phosphatase level was also significantly (p value 0.049) lower in group I (242.42±194.28 IU/L) than group II (455.67±298.29 IU/L). Serum albumin was significantly higher (p value 0.022) in group I (35.17±4.24 gm/dl) than group II (31.67±2.53 gm/dl). PT was similar in both group, group I (12.94±1.66 sec) and group II (14.05±1.25 sec).

Table 2: Preoperative liver function test between two groups

	Group-I (n=24) Mean±SD (range)	Group-II (n=24) Mean±SD (range)	p value
Serum bilirubin (mg/dl)	3.25±2.71 (0.6-9.2)	9.47±5.13 (3.8-19)	0.001[s]
Alkaline phosphatase (IU/L)	242.42±194.28 (48-660)	455.67±298.29 (140-1110)	0.049[s]
Prothombin time (sec)	12.94±1.66	14.05±1.25	0.077[ns]
Serum albumin (gm/dl)	35.17±4.24	31.67±2.53	0.022[s]

Table 3 shows difference of bacterial growth in bile between two group patients. Bacteria were isolated in 10 (83.3%) patients in group I in contrast bacteria was isolated 6 (50%) patients of group II. Although the difference wasn't significant between two groups (p value 0.083) but the incidence of bactibilia was higher in group I than group II. Polymicrobial growth in bile was significantly more (p=0.012) in group I in compare to group II patients. The most common bacteria in bile was I Klebsiella spp (60.0%) in group I (p=0.024) and E. coli in group II (p=0.386). However, the uncommon bacteria in bile (Pseudomonas spp., Proteus species and Enterobacter cloacae complex) were found only in group.

Table 3: Isolated organisms from bile

Variables	Group I (n=24)		Group II (n=24)		P Value
	n	%	n	%	
Culture positive	20	83.3	12	50.0	0.083[ns]
Culture negative	4	16.7	12	50.0	
Isolated Organisms					
Monomicrobial	10	41.7	12	50.0	0.682[ns]
Polymicrobial	10	41.7	0	0.0	0.012[s]
Klebsiella spp.	12	50.0	2	8.3	0.024[s]
E. coli	6	25.0	10	41.7	0.386[ns]
Pseudomonas spp.	4	16.7	0	0.0	0.139[ns]
Proteus species	2	8.3	0	0.0	0.307[ns]
Enterobacter cloacae complex	2	8.3	0	0.0	0.307[ns]

Table 4 shows the difference of antibiogram of bile organism between two groups of patients. Cephalosporin group of antibiotics were more resistant (50-75%) in group I than group II (16.3-33.3%). Carbapenam group of antibiotic were more sensitive in group II (100%) than group I (41.7-66.7%). Aminoglycosides has similar sensitivity (66.7%) in both groups. Colistin was 100% sensitive in both groups. The sensitivity of Amoxicillin, Ciprofloxacin and Cotrimoxazole were lower in both group.

Table 4: Antibiotic sensitivity pattern of bile culture

	Group-I			**Group-II**	
Antibiotic Group	**Antibiotic**	**Sensitivity**	**Resistance**	**Sensitivity**	**Resistance**
		n(%)	**n(%)**	**n(%)**	**n(%)**
Penicillin	Amoxicillin	8(33.3)	12(50.0)	6(50.0)	6(50.0)
	Tazobactam	18(75.0)	2(8.3)	10(83.3)	2(16.6)
Cephalosporin	Cefuroxime	4(16.7)	16(66.7)	10(83.3)	2(16.3)
	Ceftriaxone	2(8.3)	18 (75.0)	8(66.7)	4(33.3)
	Cefepime	8(33.3)	12(50.0)	10(83.3)	2(16.3)
Aminoglycosides	Amikacin	16(66.7)	4(16.7)	10(66.7)	2(16.3)
Carbapenem	Imipenem	16(66.7)	0(0.0)	12(100.0)	0(0.0)
	Meropenam	10(41.7)	10(41.7)	12(100.0)	0(0.0)
Fluoroquinolones	Ciprofloxacin	2(8.3)	12(50.0)	6(50.0)	6(50.0)
Others	Cotrimoxazole	8(33.3)	2(8.3)	4(33.3)	2(16.6)
	Colistin	20(100.0)	0(0.0)	12(100.0)	0(0.0)

Table 5 shows the incidence and type of organism isolated from SSI. Organism were isolated from16 (66.7%) patients infected wound in group I and from 6 (25%) patients in group II and the difference is statistically significant (p=0.040). This indicating strong association of SSI with ERCP stenting. E. coli is the most common organism isolated in group I (p=0.028). Among others Streptococcus, Enterococcus spp. and Streptococcus were more frequently found in group II and Klebsiella and Streptococcus in group I.

Table 5: Incidence and type organisms from surgical site infection

Variables	**Group I (n=24)**		**Group II (n=24)**		**P Value**
	n	**%**	**n**	**%**	
Organism Isolated	16	66.7	6	25.0	0.040^{s}
Organism negative	8	33.3	18	75.0	
Organism isolated					
Klebsiella	4	16.7	4	16.7	0.100^{ns}
E. coli	8	33.3	0	0.0	0.028^{s}
Enterococcus spp.	2	8.3	0	0.0	0.307^{ns}
Streptococcus	6	25.0	2	8.3	0.273^{ns}
Pseudomonas	2	8.3	0	0.0	0.307^{ns}

This table 6 illustrates (70%- 66.7%) patients with positive bile culture develop SSI which is statistically significant (p value 0.048). This clearly indicating a strong association of positive bile culture with SSI. (83.3%-50%) patients with negative bile culture didn't develop SSI.

Table 6: Relation of positive bile culture and Surgical Site Infection

	Group-I	**Group-II**			
Surgical site infection					
Bile culture	**Positive**	**Negative**	**Positive**	**Negative**	**p value**
	n(%)	**n(%)**	**n(%)**	**n(%)**	
Positive	14(70%)	6(30%)	4(66.7%)	2(33.3%)	0.048s
Negative	4(50%)	2(50%)	2(16.6%)	10(83.3%)	

Table 7 shows the difference of post-operative complication between two groups. Infectious complications were found 75% patients in group I and 41.7% in group II patients (p=0.097). Among infectious complications SSI between two group was statistically significant (p=0.040) but others (intra-abdominal abscess, ARDS, Septicemia and UTI) almost similar in two group. Non-infective complications were found 66.7% patients in group I and 58.3% in group II patients. Biliary leakage (16.7%) and Grade B (16.7%) and Grade C (16.7%) pancreatic fistula were more in Group I although statistically not significant. Another

interesting finding was that 90% of patients with Drunking type pancreaticojejunostomy developed pancreatic fistula mostly Grade A. Delayed Gastric Emptying observed in 25% mostly aged below 50 years. Mean length of Post –Operative hospital stay 17.17±8.58 in Group I and 13.33±8.26 in Group II. Mortality was 8.3% in both groups.

Table 7: Post-operative outcome between two groups

	Group-I (n=24)		Group-II (n=24)		p value
	n	%	n	%	
Infectious complications	18	75.0	10	41.7	$^{a}0.097^{ns}$
Surgical site Infection	16	66.7	6	25.0	0.040^{s}
Intra-abdominal abscess	2	8.3	2	8.3	$^{a}1.00^{ns}$
ARDS	2	8.3	2	8.3	$^{a}1.000^{ns}$
Pneumonia	4	16.7	2	8.3	$^{a}0.537^{ns}$
Septicemia	4	16.7	4	16.7	$^{a}1.00^{ns}$
UTI	6	25	4	16.7	$^{a}0.615^{ns}$
Non-infectious complications	16	66.7	14	58.3	$^{a}0.673^{ns}$
Biliary leakage	4	16.7	2	9.1	$^{a}0.537^{ns}$
Pancreatice leakage					
Grade A	6	25.0	8	33.3	$^{a}0.653^{ns}$
Grade B	4	16.7	2	8.3	$^{a}0.537^{ns}$
Grade C	4	16.7	2	8.3	$^{a}0.537^{ns}$
Haemorrhage	2	12.5	2	8.3	$^{a}1.00^{ns}$
Delayed Gastric Emptying	6	25.0	6	25.0	$^{a}1.00^{ns}$
Mean length of Post –Operative hospital stay	17.17±8.58		13.33±8.26		$^{b}0.271^{ns}$
Mortality	2	8.3	2	8.3	$^{a}1.00^{ns}$

DISCUSSION

Many studies stated that PBD improved liver function, reduced endotoxaemia and cytokine release and improved immune function (Clements *et al.*, 1996; Liu and Li 2015; Parks *et al.*, 1996) [9-11]. Other hand, some others studies stated that PBD associated with bactibilia with polymicrobial organism showing resistance to commonly used [1, 12, 13]. Studies also found that PBD correlates with more intraoperative bleeding, prolonged operation time and post- operative wound infection which increase the length of hospital stay of patient. So, the advantages of preoperative biliary drainage for patients with peri-ampullary and ampullary malignancies who are undergoing PD are still debated [14].

In our study we found significant improvement of liver function following PBD S. bilirubin (p= 0.001), Alkaline phosphatase (p= 0.049) and S. albumin (p= 0.022) although 83.3% of them have positive bile culture with significant polymicrobial growth (p value 0.036). No polymicrobial growth seen in non-stent group. Uncommon organisms (Pseudomonas spp., Proteus species, Enterobacter cloacae complex) observed in stent group. Basioukas *et al.*, & Howard *et al.*, also observered similar findings low pressure in common bile duct, loss of mechanical barrier of sphincter of oddi due to endoscopic sphincterotomy leads to duodenal content reflux may contribute to organism growth. Plastic stent also acts as a nidus for organism growth. Other striking feature in our study was absence of anaerobic bacteria; other study reported scarcity of anaerobic organisms in [15].

We also observed those organisms in stent group have higher resistant pattern to Cephalosporin and Carbapenem than non-stent group. The curious finding of this study is Colistin which was tested most of the cases, shows 100% sensitivity. Miah *et al.*, (2020) also showed similar finding in their study. This polymicrobial growth in bile and resistant antibiogram profile of stent group may responsible for this higer infection rate as we observed significant SSI in stent group (p=0.040) [12]. Similar finding was observed by Ng, Suthananthan, and Rao. We found no significant difference in other infectious complications like pneumonia, ARDS and UTI between two groups. We observed intra operative blood loss (p value 0.006) and adhesion (p value 0.001) were significant in patients with stented than non- stented group were which are similar to other studies by Miah *et al.*, (2020) and Hodul *et al.*, (2003) [12, 16]. Biliary endoprostheses-induced inflammatory responses with significant fibrosis and bile duct wall thickening might be the cause of increased preoperative blood loss and lengthier surgical periods. This inflammatory reaction causes increased vascularity in the surrounding tissues and adhesion development, making dissection around bile duct more difficult. Biliary leakage and pancreatic leakage are also significantly observed in stent group. Another observation is that whenever Drunking pancreaticojejunostomy done leakage was more (90%). Liu *et al.*, (2015) found the time between placing the biliary stent and surgery is critical because the longer

the biliary stent is in place, the longer intestinal bacteria will reflux into the biliary tree, increasing the risk of bacterial colonization [10]. We found only 75% patient went for surgery after 4 weeks of PBD. Similar t0 Miah *et al.,* (2020) found 62% [12]. This is most likely owing to poor patient counseling regarding the disease and treatment options, as well as a lack of a referral system. We found only 33.3% patients have written advice of surgery on their ERCP report. Besides this symptomatic improvement of the patients also plays a vital role in the delay process.

Some study has therefore recommended not to do biliary decompression until patients suffer from severe obstructive jaundice 15-17.5 mg/dl [10, 17]. We found 33.3% patients underwent PBD with S bilirubin <5 mg/dl, 16.6% with S bilirubin 5-10 mg/dl, 8.3% S bilirubin 10-15 mg/dl and 41.6% S bilirubin >15 mg/dl. We also found that patient underwent ERCP with low S. bilirubin experienced more complications than with higher S. bilirubin. As most of the patients of our study population underwent PBD with low S. bilirubin, we observed more complications (41.7%) following ERCP than others. This could be attributed to a lack of biliary tree dilation as a result of the shorter length of obstruction, as indicated by low S. bilirubin. On the basis of above finding and discussion it can be concluded that preoperative biliary drainage in patients with obstructive jaundice should be considered only when indicated.

CONCLUSIONS

Preoperative biliary drainage in patients with obstructive jaundice significantly improved liver function but strongly associated with polymicrobial bactibilia, antibiotic resistance, wound infection, par-operative bleeding, and adhesion. So routine biliary decompression should be considered only when deemed needed. Also strong counseling and good referral system should be developed following PBD for curative management.

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