

Original Research Article

Pancreatic Fistula Following Pancreatoduodenectomy: A Focus on Drain Amylase Dynamics and Surgical Variables

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Abstract: Introduction: Postoperative pancreatic fistula (POPF) remains one of the most challenging complications following pancreatoduodenectomy, contributing significantly to morbidity and mortality. This study explores the relationship between clinical, biochemical, and surgical factors and the development of POPF, with a focus on identifying predictors. **Methods:** This observational study was conducted in Dhaka Medical College & Hospital (DMCH), Dhaka, from January 2023 to December 2023. 30 patients with the Whipples procedure were selected as study subjects by purposive simple random sampling technique. Analysis was done manually by MS Word & MS Excel worksheet and SPSS. The unpaired t-test and Chi-square test were done for data analysis. **Result:** POPF was significantly associated with a smaller main pancreatic duct diameter (≤ 3 mm, $p = 0.006$) and soft pancreatic texture ($p = 0.00005$). Elevated drain fluid amylase levels, particularly on postoperative day 5, highlighted its role in the early detection of POPF. Periapillary carcinoma was the most common diagnosis overall, though only chronic pancreatitis showed a significant association with POPF ($p = 0.032$). The duct-to-mucosa anastomotic technique significantly reduced the risk of POPF compared to the dunking method ($p = 0.00001$). Other variables, including blood loss and procedure type, were not significantly linked to POPF development. **Conclusion:** This study highlights that postoperative pancreatic fistula (POPF) following pancreatoduodenectomy is strongly influenced by factors such as small main pancreatic duct diameter (≤ 3 mm), soft pancreatic texture, and the anastomotic technique used. Elevated drain fluid amylase levels in the early postoperative period emerged as a reliable marker for POPF risk.

Keywords: Pancreatic Fistula, Pancreatoduodenectomy, Drain Amylase, Surgical Variables.

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INTRODUCTION

Pancreaticoduodenectomy, commonly referred to as the Whipple procedure, is a complex surgical intervention often performed for malignant and benign conditions affecting the periampullary region, head of the pancreas, duodenum, and distal bile duct [1, 2]. Despite significant advancements in surgical techniques, postoperative pancreatic fistula (POPF) remains one of the most common and challenging complications following this procedure, with reported incidence rates ranging from 5% to 30% [3]. POPF not only increases morbidity and mortality but also prolongs hospital stays and escalates healthcare costs [4]. POPF is characterized

by the abnormal leakage of pancreatic enzymes from the pancreatic anastomosis site into the surrounding tissues or drains. The International Study Group on Pancreatic Surgery (ISGPS) classifies POPF based on its clinical and biochemical characteristics, highlighting its severity as a predictor of adverse outcomes [5]. Among the numerous predictive factors, drain amylase levels and pancreatic surgical variables have gained substantial attention in recent years for their ability to identify high-risk patients [6]. The measurement of drain amylase levels in the early postoperative period has become a standard practice for assessing POPF risk. A drain amylase level greater than three times the upper limit of serum amylase on postoperative day (POD) 1 is a widely

accepted marker for biochemical fistula, serving as an early indicator of anastomotic leakage [7]. Patients with persistently elevated or rising drain amylase levels often exhibit clinical POPF, necessitating closer monitoring and potential intervention. Several perioperative variables have been implicated in the development of POPF. Pancreatic duct diameter is one of the most critical anatomical factors. A narrow duct (<3 mm) poses technical challenges during anastomosis, resulting in an increased risk of leakage [8]. Pancreatic texture also plays a pivotal role, with a soft and friable pancreas being more prone to enzymatic leakage compared to a firm or hard pancreas [3, 5]. Furthermore, the choice of anastomotic technique—whether duct-to-mucosa or dunking—has shown a significant impact on fistula rates. Studies suggest that duct-to-mucosa anastomosis provides better sealing of the pancreatic duct, thereby reducing the incidence of POPF [9]. While intraoperative factors such as blood loss and operative time are considered indirect contributors, their role in the development of POPF is less well-established [10]. However, meticulous surgical technique and adherence to principles of hemostasis and tissue handling remain crucial in minimizing complications. The clinical implications of POPF are profound, ranging from localized infections and abscess formation to systemic complications such as sepsis and organ failure [11]. The presence of POPF significantly increases the likelihood of readmissions and reoperations, adversely impacting long-term oncological outcomes in patients undergoing surgery for malignancies [12]. As a result, the management of POPF often requires a multidisciplinary approach, encompassing nutritional support, drainage procedures, and in severe cases, re-exploration surgery. This study aimed to assess the predictive value of drain amylase levels and explore the role of key surgical factors, including pancreatic duct diameter, texture, and anastomotic technique, in the development of POPF.

METHODS

This observational study was conducted in Dhaka Medical College & Hospital (DMCH), Dhaka, from January 2023 to December 2023. Patients admitted to DMCH to whom the Whipples procedure was

performed within our study period were considered as the study population. 30 patients were selected as study subjects by purposive simple random sampling technique. Necessary information was obtained from history, physical examination, investigation, follow-up chart, operation note, and discharge certificates. Drain fluid amylase on day one (POD-1), day three (POD-3), and day five (POD-5), and serum amylase level on day one (POD-1), day three (POD-3) and day five (POD-5) was measured. Analysis was done manually by MS Word & MS Excel worksheet and SPSS. Unpaired t-test and Chi-square test were done for data analysis. Informed written consent was taken from participants. Ethical clearance was taken from Dhaka Medical College.

Inclusion Criteria:

- The patient underwent Pancreatoduodenectomy for various indication.
- Age between 16 to 70 years.

Exclusion Criteria:

- Patient with concomitant other malignancy.
- Patient with a history of previous upper gastrointestinal surgery.

RESULTS

Table I: Age distribution of the study population (n=30)

Age in years	Number	Percentage
21-30	01	3.3
31-40	03	10.0
41-50	11	36.6
51-60	09	30.0
> 60	06	20.0
Total	30	100.0

The majority of participants were aged 41–50 years (36.6%), followed by those aged 51–60 years (30.0%). Participants aged >60 years accounted for 20.0%, while those aged 31–40 years constituted 10.0%. The youngest age group (21–30 years) had the lowest representation, with only 3.3% [Table I].

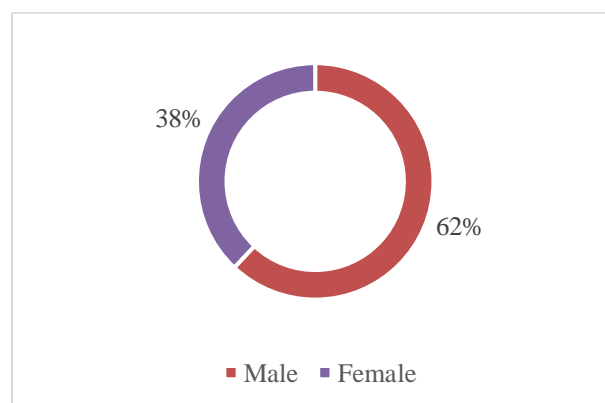


Figure 1: Sex distribution of the study population

Figure 1 shows most of the hepatobiliary malignancy is from the female (62%) group.

Table II: Mean value of pancreatic drain fluid amylase and S. amylase in POD1, POD3, POD5 (n=30)

Days	S. Amylase IU/L	Drain Fluid Amylase
*POD1	523	232
POD3	332	347
POD5	300	627

*POD- Post Operative Day

The table presents the mean values of serum amylase (S. Amylase) and pancreatic drain fluid amylase over postoperative days (POD) 1, 3, and 5. Serum amylase levels showed a gradual decline from 523 IU/L on POD1 to 300 IU/L on POD5. Conversely, drain fluid

amylase levels initially increased, rising from 232 IU/L on POD1 to 347 IU/L on POD3, followed by a sharp rise to 627 IU/L on POD5. This divergence, particularly the significant increase in drain fluid amylase on POD5 [Table II].

Table III: Patient developing biochemical fistula (Drain fluid amylase > 3x S. Amylase) (n=30)

Drain Fluid and S Amylase ratio	POD1	POD3	POD5
Drain Fluid amylase<3x S. Amylase	10	12	19
Drain Fluid amylase>3x S. Amylase	20	18	11

The table describes the number of patients developing biochemical pancreatic fistula, defined as drain fluid amylase levels exceeding three times the serum amylase (S. Amylase) levels, across postoperative days (POD) 1, 3, and 5. On POD1, 20 patients (66.7%) had drain fluid amylase >3x S. Amylase, which

decreased to 18 patients (60%) on POD3 and further to 11 patients (36.7%) on POD5. Conversely, the number of patients with drain fluid amylase <3x S. Amylase increased from 10 (33.3%) on POD1 to 19 (63.3%) by POD5 [Table III].

Table IV: Distribution of the diagnosis among the samples, between two groups, group 1 with POPF and group 2 without POPF (n=30)

Diagnosis	Group1 (n=6)	Group 2 (n=24)	P-value
Periampullary carcinoma	01	15	0.1
Ca Head of Pancreas	03	04	0.147
Cholangiocarcinoma	01	04	0.324
Duodenal malignancy	01	00	0.05
Chronic Pancreatitis	00	01	0.032

Group 1 (patients with postoperative pancreatic fistula, POPF) and Group 2 (patients without POPF), were among the 30 study participants. Periampullary carcinoma was the most common diagnosis, seen in 1 patient (16.7%) in Group 1 and 15 patients (62.5%) in Group 2, with a non-significant p-value of 0.1. Carcinoma of the head of the pancreas was observed in 3

patients (50%) in Group 1 and 4 patients (16.7%) in Group 2 (p = 0.147). Cholangiocarcinoma and duodenal malignancy showed no statistically significant association with POPF, with p-values of 0.324 and 0.05, respectively. Chronic pancreatitis was rare and only seen in 1 patient from Group 2, with a significant p-value of 0.032 [Table IV].

Table V: Comparison of Perioperative variables among two groups (n=30)

Variables		Group 1 (n=6)	Group 2 (n=24)	P-value
MPD diameter	0-3	3	04	.006
	4-6	2	10	
	>6	1	10	
Pancreatic texture	Soft	04	03	.00005
	Firm	01	16	
	Hard	01	05	
Procedure	Classical	06	23	0.596
	PPPD*	00	01	
Blood loss	<300	02	04	0.704
	300-500	02	06	
	>500	02	14	
Anastomotic technique	Ducto-mucosal	02	20	0.00001
	Dunking	04	04	

*PPPD-Pylorus-Preserving Pancreatoduodenectomy

A smaller main pancreatic duct (MPD) diameter (0–3 mm) was significantly associated with POPF ($p = 0.006$), as it was present in 50% of patients in Group 1 compared to only 16.7% in Group 2. Pancreatic texture also emerged as a strong predictor, with soft texture significantly more common in patients with POPF (66.7% in Group 1 vs. 12.5% in Group 2, $p = 0.00005$). The type of procedure performed, whether classical pancreatoduodenectomy or PPPD, showed no significant association with POPF ($p = 0.596$). Similarly, blood loss during surgery was not significantly linked to POPF ($p = 0.704$). However, the anastomotic technique played a crucial role, with the duct-to-mucosa method being significantly less associated with POPF compared to the dunking technique ($p = 0.00001$) [Table V].

DISCUSSION

The age distribution in this study revealed a predominance of patients in the 41-50 and 51-60 age groups, which is consistent with earlier reports showing that pancreaticobiliary malignancies typically affect middle-aged to older adults [13]. The youngest cohort (21-30 years) was notably underrepresented, with only one patient in this age group, reinforcing the observation that pancreatic diseases, including malignancies, are less common in younger individuals. Furthermore, the study observed a higher incidence of pancreaticobiliary malignancies in females, with 62% of the study population being female. This gender distribution is in line with prior studies that have shown a slight female predominance in various hepatobiliary and pancreatic cancers [2]. Amylase levels in pancreatic drain fluid are widely regarded as a reliable biomarker for predicting POPF [14]. In this study, serum amylase levels showed a gradual decline from POD1 to POD5, which is consistent with the physiological progression after surgery. While serum amylase decreased, drain fluid amylase initially increased on POD3 and exhibited a sharp rise on POD5. This pattern suggests the presence of a reactive process, where pancreatic secretion continues despite the absence of a complete healing process in pancreatic anastomosis, a phenomenon that has been previously reported [5]. The development of a biochemical pancreatic fistula, as defined by drain fluid amylase levels greater than three times the serum amylase levels, was evident in a significant proportion of patients. On POD1, 66.7% of patients had a drain fluid amylase $>3x$ serum amylase, which decreased over time. This finding aligns with earlier studies suggesting that elevated amylase in drain fluid during the early postoperative period is indicative of pancreatic leak and correlates with the eventual development of POPF [15, 16]. Remarkably, by POD5, only 36.7% of patients exhibited drain fluid amylase $>3x$ serum amylase, suggesting a potential resolution or containment of the leak. Regarding the distribution of diagnoses between groups with and without POPF, the most common diagnosis in both groups was periampullary carcinoma. While periampullary carcinoma was observed in 62.5% of the non-POPF group, it was seen in only 16.7% of the POPF group,

although the difference was not statistically significant ($p = 0.1$). Carcinoma of the head of the pancreas, which is closely associated with periampullary carcinoma, was the second most common diagnosis. This observation is consistent with the literature, where pancreatic ductal adenocarcinoma (PDAC) is the most frequent cause of pancreaticobiliary surgery [17]. Chronic pancreatitis was more commonly found in patients without POPF, supporting the hypothesis that softer pancreatic textures seen in chronic pancreatitis may contribute to reduced leakage rates postoperatively [18, 19]. Several perioperative variables were assessed for their association with the development of POPF. A significant association was found between a smaller main pancreatic duct (MPD) diameter (0-3 mm) and the occurrence of POPF ($p = 0.006$). This finding aligns with previous studies indicating that a smaller MPD is a strong predictor of pancreatic leak, as smaller ducts are more prone to injury during surgery and may not provide adequate drainage for pancreatic enzymes [5]. Notably, the type of procedure (Classical PD vs. PPPD) did not show a significant association with POPF ($p = 0.596$), suggesting that, in this cohort, the procedure type might not be as influential in determining the risk of POPF. However, this finding is contrary to some studies that have suggested a lower risk of POPF in PPPD procedures due to the preservation of the duodenum and its potential effects on pancreatic secretion and healing [8]. The anastomotic technique, however, played a crucial role in reducing POPF risk. The duct-to-mucosa anastomosis technique was significantly less associated with POPF compared to the dunking technique ($p = 0.00001$), supporting the growing body of evidence that duct-to-mucosa anastomosis leads to better outcomes in terms of fistula prevention [20].

Limitations of The Study

The study was conducted in a single hospital with a small sample size. So, the results may not represent the whole community.

CONCLUSION

This study highlights that postoperative pancreatic fistula (POPF) following pancreatoduodenectomy is strongly influenced by factors such as small main pancreatic duct diameter (≤ 3 mm), soft pancreatic texture, and the anastomotic technique used. Elevated drain fluid amylase levels in the early postoperative period emerged as a reliable marker for POPF risk. While variables like blood loss and procedure type showed no significant correlation, duct-to-mucosa anastomosis was associated with a reduced POPF risk.

RECOMMENDATION

To reduce the risk of postoperative pancreatic fistula (POPF) following pancreatoduodenectomy, we recommend a preoperative assessment of pancreatic duct diameter and texture to identify high-risk patients.

Intraoperative strategies should prioritize duct-to-mucosa anastomosis for pancreatic reconstruction, as it is associated with a lower incidence of POPF. Early postoperative monitoring of drain fluid amylase levels is essential for timely identification and management of biochemical fistula. Further research should focus on optimizing surgical techniques.

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