

# Factors Correlated with Post Endoscopic Retrograde Cholangiopancreatography Hyperamylasemia: A Single Center Study

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## ABSTRACT

**Background and aim of the work:** Identifying patient at risk for post ERCP hyperamylasemia which may progress to pancreatitis is essential to minimize morbidity and mortality by suitable procedural or pharmacological intervention. In this study hyperamylasemia following ERCP were recorded and correlated with different patient or procedure related risk factors.

**Patients and methods:** The data of all patients who met the inclusion criteria of the study and underwent endoscopic retrograde cholangiopancreatography (ERCP) in Al-Hada Armed Force Hospital, Taif, Saudi Arabia from January 2015 to March 2016, were collected through a review of their hospital and data base records.

**Results:** There were 138 patients (86 females and 52 males) with mean age of  $63.7 \pm 15.3$  years. Hyperamylasemia was developed in 29.7% of them; 16.8% were recorded as asymptomatic hyperamylasemia and post ERCP pancreatitis in the remaining 13%. Multivariate analysis confirmed that, the gender, precut sphincterotomy and pancreatic duct cannulation were significant risk factors for development of non symptomatic hyperamylasemia and confirmed also the significance of precut sphincterotomy and pancreatic duct cannulation for post ERCP pancreatitis.

**Conclusion:** This study confirmed the correlation of precut sphincterotomy and pancreatic duct cannulation with post ERCP hyperamylasemia and pancreatitis and in such conditions preventive measures are recommended.

**Keywords:** post ERCP, Hyperamylasemia, pancreatitis, Risk Factors.

## INTRODUCTION

Hyperamylasemia following ERCP is recorded in more than seventy percent of patients following the procedure, however, only 3.5-15% would be symptomatic with evident post ERCP pancreatitis (PEP) [1-5]. This wide variation in the incidence of post ERCP pancreatitis would be attributed to the associated risk factors [2, 6]. These risk factors vary from one study to another and may be patient related risk factors as; female sex, young age, history of PEP, and absence of hyperbilirubinemia [3, 5, 7].

Most of the procedure related risk factors are related to difficult endoscopic intubation that lead to injury of pancreatic tissues or edema with duct obstruction and consecutive pancreatitis [1, 2, 8-10]. Risky measures used during intubation include; difficult cannulation with repeated or deep wiring, precut sphincterotomy, and prolonged cannulation of the pancreatic duct [1-5, 9]. Few studies considered dysfunction of sphincter of Oddi as a risk factor; however, synergistic cofactors are usually found [3, 4, 9, 10].

The objective of this study and similar studies is to identify patients at risk and reduce morbidity and mortality of PEP if suitable preventive measures are used [1, 12-15]. In this study hyperamylasemia following ERCP were recorded and correlated with different patient or procedure related risk factors.

### Method:

In this retrospective study the patients who underwent endoscopic retrograde cholangiopancreatography (ERCP) in Al-Hada Armed Force Hospital, Taif, Saudi Arabia from January 2015 to march 2016 were identified in the computerized hospital database registration system. One hundred thirty eight patients met the inclusion criteria which included; the patients who were admitted with normal amylase level

and this level increased following performance of ERCP with or without associated clinical, laboratory or imaging evidence of development of post ERCP pancreatitis. Exclusion criteria included; patients with elevated serum amylase or evident pancreatitis at time of admission, incomplete and unclear files.

### Ethical approval:

**After approval of the ethics committee;** the records were reviewed for the patient specific risk factors at time of admission as; gender, age group, bilirubin level, diameter of the common bile duct, presence of choledocholithiasis, in addition to factors related to the procedure as; precut sphincterotomy, pancreatic duct cannulation, depth of cannulation and procedure time.

The collected data were analysed using SPSS version 22 (IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp). The data was expressed as means  $\pm$ SD and percentage. A univariate and multivariate logistic regression analyses of patient specific and procedure related factors were performed to identify factors associated with development of post ERCP hyperamylasemia with or without evident pancreatitis.  $P < 0.05$  was considered as statistically significant.

## RESULTS

There were 138 patients (86 females and 52 males) with mean age of  $63.7 \pm 15.3$  years. Hyperamylasemia was developed in 41 patients (29.7%). Twenty three/138 patients were asymptomatic (16.7%) and in 18/138 (13%) pancreatitis were confirmed. Table 1, shows the relation of assumed risk factors and non symptomatic hyperamylasemia. Table 2, shows the relation of these factors and post ERCP pancreatitis.

**Table 1:** relation of assumed risk factors and non symptomatic hyperamylasemia

Assumed risk factors	variables	
Gender	Male: 6/52 (11.5%)	Female: 17/86 (19.8%)
Age group (mean in years)	Below 40 (31.5±6.2): 3/32 (9.4%)	Above 40 (71.6±16.4): 20/106 (18.9%)
Bilirubin	Elevated: 21/101 (20.8%)	Normal: 2/37 (5.4%)
Common bile duct	Not dilated: 15/78 (19.2%)	Dilated: 8/60 (13.3%)
CBD stone	Present: 9/70 (12.9%)	Absent: 14/68 (20.6%)
Precut sphincterotomy	Done: 20/108 (18.5%)	Not done: 3/30 (10%)
Pancreatic duct cannulation	Done: 7/21 (33.3%)	Not done: 16/117 (13.7%)
Depth of cannulation	Incomplete data	
Time of manipulation	Incomplete data	

**Table 2:** relation of assumed risk factors and post ERCP pancreatitis

Assumed risk factors	variables	
Gender	Male 6/52 (11.5%)	Female 12/86 (14%)
Age group (mean in years)	Below 40 (31.5±6.2) 2/32 (6.3%)	Above 40 (71.6±16.4) 16/106 (15.1)
Bilirubin	Elevated: 14/101 (13.9%)	Normal: 4/37 (10.8%)
Common bile duct	Not dilated: 8/78 (10.3%)	Dilated: 10/60 (16.7%)
CBD stone	Present: 11/70 (15.7%)	Absent: 7/68 (10.3)
Precut sphincterotomy	Done: 13/108 (12%)	Not done: 5/30 (16.7%)
Pancreatic duct cannulation	Done: 6/21 (28.6)	Not done: 12/117 (10.3%)
Depth of cannulation	Incomplete data	
Time of manipulation	Incomplete data	

**Table 3:** Multivariate analysis of the assumed risk factors for asymptomatic hyperamylasemia

Variables	Multivariate analysis		
	P-value	OR	CI 95%
Pre cut sphincterotomy	<0.001 (S)	1.016	1.118–1.395
Pancreatic duct dilatation	<0.001 (S)	1.077	1.243-1.606
Gender	0.002 (S)	1.032	1.317-1.464
Bilirubin level	0.053 (IS)	1.422	0.614–1.206
Age group (below 40 years)	<0.061(IS)	1.032	1.434-1.547

OR; Odds Ratio, CI; Confidence Interval, S; Significant, IS; Insignificant

Univariate analysis found that female gender, young age, bilirubin level before ERCP, performance of precut sphincterotomy during ERCP, and pancreatic duct cannulation were significant independent variables ( $P < 0.05$ ). Other variables (common bile duct diameter and CBD stone) were insignificant ( $P > 0.05$ ). After controlling for confounders in multivariate logistic regression analysis; only precut sphincterotomy, pancreatic duct cannulation, and female gender were confirmed to be significant, whereas, age group and bilirubin level were found to be insignificant (Table 3).

**Table 4:** Multivariate analysis of the assumed risk factors for post ERCP pancreatitis

Variables	Multivariate analysis		
	P-value	OR	CI 95%
Precut sphincterotomy	<0.001 (S)	1.002	1.227-1.507
Pancreatic duct dilatation	0.002 (S)	1.065	1.371-1.515
Young age (below 40 years)	0.073 (IS)	1.034	1.009–1.947

OR; Odds Ratio, CI; Confidence Interval, S; Significant, IS; Insignificant

Univariate analysis found that, precut sphincterotomy, pancreatic duct cannulation, and age below 40 years were significant independent variables ( $P < 0.05$ ) for post ERCP pancreatitis and the other variables were insignificant ( $P > 0.05$ ). However; after controlling for confounders in multivariate logistic regression analysis; only precut sphincterotomy and pancreatic duct cannulation were confirmed to be significant (Table 4).

## DISCUSSION

Hyperamylasemia is a common finding after ERCP; however, symptomatic cases and cases associated with marked rise in amylase level or lipase, namely the post ERCP pancreatitis are serious but less common conditions [1-3]. Determination of risk factors for hyperamylasemia and PEP would help identifying risky patients and the use of preventive pharmacological or technical measures [1, 12-15]. Even though, the cause of these complications in some patients remains unclear [8-10]. The results of this report confirmed the findings of previous similar studies which found that hyperamylasemia and post ERCP pancreatitis are correlated with difficult pancreatic cannulation especially if a guide wire is deeply and repeatedly passed or/and a precut sphincterotomy is used [1-3, 10]. However, the results of this study may be limited by the lack of data about depth and time of cannulation. Mild pancreatic injury is usually related to asymptomatic hyperamylasemia; however, more severe injury would produce extensive inflammatory response resulting in PEP [7, 9, 11]. Repeated cannulation would injure the papilla leading to papillary edema and sphincter spasm that obstructs the flow of pancreatic secretions resulting in variable degrees of inflammatory response that lead to hyperamylasemia with/without evident pancreatitis [1-7]. Precut sphincterotomy is used by endoscopists to facilitate cannulation and is considered by **Ding et al.** in their meta-analysis as a highly significant risk factor for pancreatitis after ERCP [1]. The results of the present study are similar. **Talukdar** evaluated precut techniques as; trans-pancreatic precut, needle-knife precut, and fistulotomy and found that the latter was the most significant risk factor for hyperamylasemia and pancreatitis [2]. **Rustagi and Jamidar** emphasized that fistulotomy needs to be implemented early by a skillful endoscopist to minimize adverse events [3]. Similar findings were reported by **Testoni et al.** [10].

**Freeman et al.** found that the risk of pancreatitis in a female is 18% [4]. In this study the risk of hyperamylasemia was significantly correlated with female gender, however, this factor is not correlated with PEP. The present study found no significant correlation between hyperamylasemia or PEP and patient age. Few studies reported that PEP is more common in young patients explaining that by the gradual decrease of pancreatic secretion with advance in age [1].

There is no gold standards for prevention of post ERCP hyperamylasemia and pancreatitis; however, about 40 pharmacologic agents have been studied especially nonsteroidal anti-inflammatory drugs (NSAIDs) and early results suggest the significant benefit of a single-dose rectal indomethacin or diclofenac immediately after ERCP to reduce the risk of PEP [10-15].

**Philip et al.** concluded in their study that the risk of PEP can be significantly reduced by prophylactic pancreatic stenting, which is a safe and feasible procedure [16]. Similar findings have been reported by other authors [17-18].

## CONCLUSION

This study confirmed the correlation of precut sphincterotomy and pancreatic duct cannulation with post ERCP hyperamylasemia and pancreatitis and in such conditions preventive measures are recommended.

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