ORIGINAL ARTICLE

Role of "HinCh Score" as a Non-invasive Predictor of Post-endoscopic Retrograde Cholangiopancreatography Cholangitis

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Abstract

Introduction: Post-endoscopic retrograde cholangiopancreatography (ERCP) cholangitis (PEC) is associated with increased morbidity and mortality in patients ERCP. The aim of the present study was to analyze the predictors of PEC and to formulate a predictive model for early diagnosis and management.

Materials and methods: It was a cross-sectional study that was carried out at the Sindh Institute of Urology and Transplantation from September 2019 to June 2021. All patients aged between 18 and 75 years and undergoing ERCP due to obstructive jaundice were included. Patients with altered biliary anatomy, history of hepatobiliary surgery, and concurrent sepsis were excluded. Endoscopic retrograde cholangiopancreatography intervention was performed by an expert gastroenterologist. Laboratory parameters (total leukocyte count, total bilirubin, alanine transaminase) and patient temperature were checked on admission, at 12 hours, 24 hours, and 36 hours after ERCP to document PEC.

Results: A total of 349 patients were included in the study. Among them, 176 (50.4%) patients were males. Common bile duct (CBD) stricture was the most common indication of ERCP seen in 148 (42.4%) patients followed by CBD stone and cholangiocarcinoma in 108 (30.9%) and 48 (13.8%) patients, respectively. The most common presenting complaint was jaundice noted in 300 (86%) patients followed by right hypochondrial pain in 280 (80.2%) and weight loss in 194 (55.6%) patients, respectively. Post-ERCP cholangitis developed in 251 (71.9%) patients. On univariate analysis, age >50 years, female gender, right hypochondrial pain, fever, bilirubin >5 mg/dL on admission, CBD stricture on ERCP, TLC of >10,000 cells/L at 12 hours, 24 hours, and 36 hours post-ERCP and rise in ALT >50 IU 24 and 48 hours post-ERCP were significantly associated with PEC. While on multivariate analysis, female gender, bilirubin >5 mg/dL on admission, CBD stricture on ERCP, post-ERCP fever, and rise in TLC of > 10000 cells/L at 24 hours post-ERCP were independently associated with PEC. HinCh score was formulated and was found to be significantly associated with the presence of cholangitis. Area under the receiver operating characteristics (AUROC) of HinCh score was 0.74 and at cutoff of ≥4, the sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of HinCh were 81.67%, 59.18%, 83.67%, and 55.71%, respectively with a diagnostic accuracy of 75.36%.

Conclusion: The performance of HinCh score in predicting PEC was accurate in 86% of the patients. However, further studies are needed to validate the score.

Keywords: Endoscopic retrograde cholangiopancreatography, HinCh score, Post-ERCP cholangitis.

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Introduction

Endoscopic retrograde cholangiopancreatography is a significant diagnostic and therapeutic tool for hepatobiliary and pancreatic diseases, which include biliary and pancreatic duct stones, biliary strictures, chronic pancreatitis, and malignancies.[1–3] Apart from its advantages, there are certain complications associated with this procedure including pancreatitis, perforation, hemorrhage, cholangitis, cholecystitis, and cardiopulmonary complications. Although the incidence of complications is 5–10%, among this, PEC is associated with high morbidity and mortality.[2,3] Tan et al.[4] documented up to 10% of mortality due to cholangitis.

Post-ERCP cholangitis is diagnosed as post-ERCP fever (temperature >38°C), jaundice, or elevated leukocytes.[5] The underlying mechanism of cholangitis can be attributed to contamination of the biliary system by gastrointestinal flora. Joshua Tierney et al.[6] reported a 13.2% incidence of PEC in 166 patients. While, Nayab et al.,[7] the only study in Pakistan pertaining to cholangitis, stated 4.9% PEC (n = 102). Chen et al.[5] predicted that age, hypertension (33%), diabetes (13%), previous ERCP history (53.9%), biliary stent insertion (45%), pancreatography (1.9%), endoscopic sphincterotomy (28.4), balloon dilation (35%), and hilar obstruction (38%) were risk factors associated with PEC. Prevention, diagnosis, and timely treatment of cholangitis are essential to avoid dreadful complications including septicemia, hepatic abscesses, liver failure, and acute renal failure.[8]

The aim of the present study was to analyze the predictors of PEC and to formulate a predictive model for early diagnosis and management.

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Materials and Methods

All patients undergoing index ERCP from September 2019 to September 2021 at Sindh Institute of Urology and Transplantation were enrolled in the study. All patients aged between 18 and 75 years who underwent ERCP for the first time were included in the study, while patients with altered biliary anatomy, history of hepatobiliary surgery, and concurrent sepsis were excluded. The initial presentation, clinical signs and symptoms, medical history, treatment duration, ERCP findings, and baseline variables including complete blood count, liver function tests, and renal function tests were recorded for each patient. Endoscopic retrograde cholangiopancreatography intervention was performed by an expert gastroenterologist. Post-ERCP, laboratory parameters including total leukocyte count and liver enzymes, and clinical parameters such as fever and abdominal pain were further recorded at 12 hours, 24 hours, and 36 hours to document the development of PEC.

Post-ERCP Cholangitis[9]

Acute cholangitis was labeled if at least 3 out of the following were present within 36 hours of ERCP.

Clinical parameters:

- New onset right upper abdominal pain

Laboratory parameters:

- Rise in temperature >38°C/100.4°F
- Rise in white blood cells <4 or >10 × 10^9/L
- Rise in total bilirubin >2 mg/dL.

Statistical Analysis

All data were analyzed by using SPSS software version 23. The quantitative data were analyzed using the Student *t*-test, while the Chi-square test was for qualitative data. The risk factors related to PEC were analyzed by univariate and multivariate analysis. Multivariate logistic regression analysis was used to estimate the independent predictors of cholangitis. A *p*-value of ≤0.05 was considered statistically significant.

HinCh score was formulated using significant variables on multivariate regression analysis and ROC was obtained for the HinCh score. A cut-off value of ≥4 was taken, at which the sensitivity, specificity, PPV, NPV, and diagnostic accuracy were calculated for the role of HinCh score in predicting PEC.

Results

A total of 349 patients who underwent ERCP for the first time were included in the study. Among them, 180 (51.6%) were males, while 169 (48.4%) were females. The mean age was 47.1 ± 13.4 years. The most common presenting complaint was jaundice noted in 300 (86%) patients followed by right hypochondrial pain in 280 (80.2%) and weight loss in 194 (55.6%) patients, respectively. The most common indication for ERCP was choledocholithiasis noted in 124 (35.5%) followed by CBD stricture in 118 (33.8%) patients. Difficult biliary cannulation was noted in 188 (53.9%) patients. Papillotomy was performed in 201 (57.6%) patients while 62 (17.8%) patients underwent sphincteroplasty. Common bile duct stenting was done in 327 (93.7%) patients. Post-ERCP cholangitis was developed in 251 (71.9%) patients. Among them, most of them were females. Post-ERCP fever was developed in 154 (44.1%) patients. A comparison of continuous and categorical variables in terms of cholangitis is shown in Tables 1 and 2, respectively. On univariate analysis, female gender, preoperative jaundice, and right hypochondrial pain, increased bilirubin on admission, dilated CBD on ERCP, CBD stricture on ERCP, post-ERCP fever, and rise in TLC of >10 × 10^9/L at 12, 24, and 48 hours post-ERCP were significantly associated with PEC. On multivariate analysis, female gender, total bilirubin >5 mg/dL on admission, CBD stricture, post-ERCP fever, and rise in TLC of >10 × 10^9 cells/L 24 hours post-ERCP were significantly associated with PEC (Table 3).

Table 1: Comparison of continuous variables in terms of cholangitis

Variable	*Cholangitis (n = 251) Mean ± SD*	*Non-cholangitis (n = 98) Mean ± SD*	*p-value*
Age	46.3 ± 13.3	10.9 ± 9.9	0.081
TLC on admission	10.9 ± 5.1	9.9 ± 3.3	0.07
TLC at 12 hours post-ERCP (10^9/L)	13.2 ± 6.6	11.2 ± 3.3	**0.004**
TLC at 24 hours post-ERCP (10^9/L)	14.5 ± 5.9	12.3 ± 3.9	**0.001**
TLC at 36 hours post-ERCP (10^9/L)	14.9 ± 5.5	13.3 ± 4.6	**0.001**
Bilirubin on admission	10.4 ± 7.3	6.1 ± 4.9	**≤0.001**
Bilirubin at 12 hours post-ERCP	9.7 ± 3.5	9.9 ± 5.45	0.915
Bilirubin at 24 hours post-ERCP	8.4 ± 2.2	8.1 ± 3.7	0.534
Bilirubin at 36 hours post-ERCP	7.6 ± 3.2	9.5 ± 5.98	0.896
ALT at admission	56 ± 62	47 ± 51	0.258
ALT at 12 hours post-ERCP	56 ± 62	47 ± 51	0.505
ALT at 24 hours post-ERCP	59.6 ± 94	52 ± 91	0.139
ALT at 36 hours post-ERCP	55 ± 66	44 ± 42	0.125
AST at admission	56 ± 81	57 ± 50	0.896
AST at 12 hours post-ERCP	64 ± 138	53 ± 40.6	0.431
AST at 24 hours post-ERCP	53 ± 70	50 ± 39	0.665
AST at 36 hours post-ERCP	51 ± 59	56 ± 35	0.885

Bold values are that of significant *p*-values (≤0.001)

Table 2: Comparison of categorical variables in terms of cholangitis ($n = 349$)

Variable	*Cholangitis (n = 251) n (%)*	*Non-cholangitis (n = 98) n (%)*	*p-value*
Gender			
Male	106 (42.2)	74 (75)	≤**0.001**
Female	145 (57.8)	24 (25)	
CBD stricture on ERCP			
Yes	127 (50.5)	75 (76)	≤**0.001**
No	124 (49.5)	23 (24)	
Stent placement			
Yes	147 (58.5)	51 (52)	0.139
No	104 (41.5)	47 (48)	
Dilated CBD on ERCP			
Yes	191 (76)	76 (77)	≤**0.001**
No	60 (24)	22 (23)	
Difficult cannulation			
Yes	128 (51)	63 (64)	0.155
No	123 (49)	35 (36)	
Papillotomy			
Yes	147 (58.5)	54 (55)	0.745
No	104 (41.5)	44 (45)	
Sphincteroplasty			
Yes	39 (15.5)	23 (24)	0.08
No	212 (84.5)	75 (76)	
Biliary stent placement			
Yes	234 (93.2)	93 (95)	0.564
No	17 (6.8)	5 (5)	
Jaundice on presentation			
Yes	209 (83.2)	91 (92.8)	**0.02**
No	42 (16.8)	7 (7.2)	
Post-ERCP fever			
Yes	128 (51)	67 (68.3)	**0.003**
No	123 (49)	31 (31.6)	
Abdominal pain on presentation			
Yes	219 (87.2)	61 (62.2)	≤**0.001**
No	32 (12.8)	37 (37.8)	

Bold values are that of significant *p*-values (≤0.001)

Table 3: Shows multivariate analysis of variables in predicting cholangitis in patients undergoing ERCP

			CI (95%)	
Variables	*p-value*	*Odds ratio*	*Lower limit*	*Upper limit*
Female gender	≤**0.001**	6.64	3.2	13.6
Presence of jaundice on admission	0.092	2.43	0.87	6.8
Total bilirubin >5 mg/dL on admission	≤**0.001**	3.65	1.67	8.002
TLC $>10 \times 10^9$ cells/L at 24 hours post-ERCP	**0.01**	0.803	0.06	0.916
TLC $>10 \times 10^9$ cells/L at 36 hours post-ERCP	0.09	1.13	0.98	1.3
CBD stricture on ERCP	≤**0.001**	0.12	0.05	0.252
Post-ERCP fever	**0.01**	0.45	0.25	0.84
Post-ERCP abdominal pain	0.06	0.5	0.24	1.05

Bold values are that of significant *p*-values (≤0.001)

Table 4: Variables incorporated in HinCh score with allotted points (total points = 8)

	Cholangitis			
Variable	*Yes*	*No*	*p-value*	*Points allotted (total = 8)*
Female gender				
Present	145	24	≤**0.001**	3
Absent	106	74		
Total bilirubin >5 mg/dL on admission				
Present	164	81	≤**0.001**	2
Absent	87	17		
CBD stricture				
Present	124	23	≤**0.001**	1
Absent	127	75		
Post-ERCP fever				
Present	123	31	≤**0.001**	1
Absent	128	67		
Rise in TLC (TLC >10×10^9/L) at 24 hours post-ERCP				
Present	132	35	**0.01**	1
Absent	119	63		

Bold values are that of significant *p*-values (≤0.001)

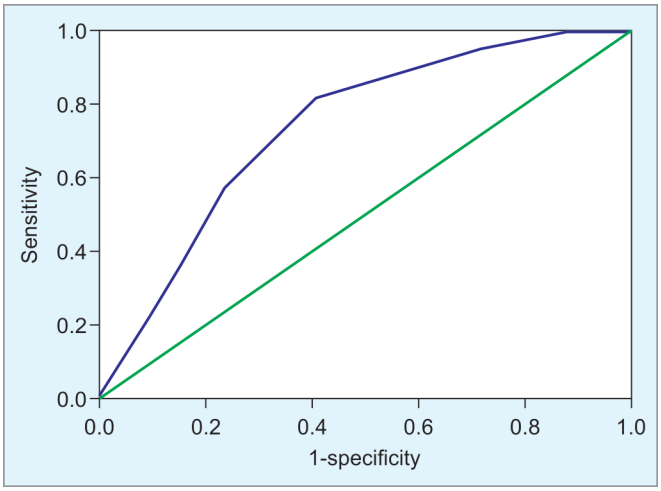

Fig. 1: Area under ROC for HinCh score in predicting PEC-0.74 (≤0.001)

Table 5: Chi-square showing significant association of HinCh score ≥4 with development of PEC

	Cholangitis		
HinCh score	*Yes*	*No*	*p-value*
≥4	204	40	≤**0.001**
<4	47	58	

Bold value is that of significant *p*-values (≤0.001)

Table 6: Shows sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of HinCh score in predicting PEC

Diagnostic accuracy	
Sensitivity	81.6%
Specificity	59.1%
PPV	83.6%
NPV	55.7%
Diagnostic accuracy	75.36%

Hence, HinCh score was formulated with a total of eight points with one point each given to each statistically significant variables; CBD stricture, post-ERCP fever, and rise in TLC of >11 × 10^9 cells/L 24 hours post-ERCP, while total bilirubin >5 mg/dL on admission was given 2 points, and female gender was given 3 points (Table 4). HinCh score was calculated and AUROC obtained for HinCh score was 0.74 and was found to have a statistically significant association in prediction of PEC (*p*-value <0.001) (Fig. 1) (Table 5). At a cutoff score of ≥4, the sensitivity, specificity, PPV, and NPV of HinCh were 81.67%, 59.18%, 83.67%, and 55.71%, respectively with a diagnostic accuracy of 75.36% (Table 6).

Discussion

The incidence of infectious complications after ERCP have been widely studied with approximately 27% rates of transient bacteremia after ERCP and rare incidence of PEC accounting for approximately less than 1% likely as a result of ineffective biliary drainage during ERCP.[10,11] In our study, PEC was noticed in 251 (63%) with most of them being females. This is largely due to the fact of delayed presentation of the patients to our department after the onset of jaundice, with the most common etiology being malignancy. In our study, we found that long history of the presence of pre-operative jaundice with high bilirubin was associated with PEC. In the previous studies, the diagnosis of malignancy on ERCP was also significantly associated with PEC.[12]

We used The Tokyo guidelines for the diagnosis of PEC. It is based on three parameters, including systemic inflammation, cholestasis, and etiology suggestive of imaging.[9] The patients included in our study fulfilled the above-mentioned criteria.

We found that in our study, the patients who had biliary stricture were most likely to develop PEC. This is likely due to the fact that the patients with prolonged stasis are more likely to have cholangitis when biliary intervention is performed as evident by high serum total leukocyte levels and rise in liver enzymes post-ERCP.[13,14]

In our study, we noticed that patients with advanced age (i.e., age >50 years) were likely to develop PEC. Similar findings were also seen in some previous studies. This is likely due to the fact that in advanced age malignancies are common, leading to cachexia and malnutrition resulting in impaired immune response.[15] Previously, ERCP performed for other etiologies such as choledocholithiasis was not associated with the development of PEC, which is also validated by our study.

By combining these significant risk factors for PEC, we formulated a score named on the initials of the primary author as "HinCh' score on the basis of multivariate analysis. One point each was given to each statistically significant variables; CBD stricture, post-ERCP fever, and rise in TLC of $>10 \times 10^9$ cells/L 24 hours post-ERCP, while total bilirubin >5 mg/dL on admission was given 2 points, and female gender was given 3 points. The score of ≥4 were found to be significantly associated with PEC with a good sensitivity of 81.67%. Although, this score lacked the specificity in predicting PEC but had a fair diagnostic accuracy of 75.36%.

This study is an important addition to the literature regarding complications of endoscopic biliary stenting. Previously, only a few studies have reported on the risk factors for PEC. There are several strengths to this study. The first and foremost is the prediction of a novel non-invasive score in predicting PEC rendering prophylactic antibiotic treatment in high-risk populations. Secondly, the prospective nature of the study allowed the proper monitoring of the follow-up of the patient.

However, there are certain limitations to our study. At first, our data lacked the ability to differentiate between benign and malignant strictures. Secondly, only derivation has been done and this score has not been validated. Lastly, a small sample size is the limitation.

Conclusion

The performance of HinCh score in predicting PEC was accurate in 75.6% of the patients. Hence, we propose its usage in endoscopy units in order to diagnose those patients who are potentially at risk of developing PEC. However, further studies comprising a larger sample size are required to validate the score.

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