Journal of
Babol University of Medical Sciences
JBUMS
e-ISSN: 2251-7170 p-ISSN: 1561-4107

Risk Factors for Markedly Elevated Aminotransferases in Patients with Common Bile Duct Stones

J. Shokri Shirvani (MD)[1], P. Akbari Shahabi (MD) [2], H. Gholinia (MSc)[3], C. Behzad (MD)[*1]

1.Clinical Research Development Unite of Rouhani Hospital, Babol University of Medical Sciences, Babol, I.R.Iran.
2.Student Research Committee, Babol University of Medical Sciences, Babol, I.R.Iran.
3.Health Research Institute, Babol University of Medical Sciences, Babol, I.R.Iran.

***Corresponding Author: C. Behzad (MD)**
Address: Clinical Research Development Unite of Rouhani Hospital, Babol University of Medical Sciences, Babol, I.R.Iran.
Tel: +98 (11) 32238301. **E-mail:** catherinebehzad@yahoo.com

Article Type
Research Paper

Received:
Jun 16th 2025
Revised:
Jun 23rd 2025
Accepted:
Jul 21st 2025

ABSTRACT

Background and Objective: Elevated liver transaminases, including alanine aminotransferase (ALT) and aspartate aminotransferase (AST), are helpful in the diagnosis of liver diseases and injuries. Marked elevation of these enzymes is most frequently observed in hepatocellular injury. In biliary tract disorders and cholestasis, aminotransferase levels typically do not rise significantly. An exception to this pattern is biliary obstruction resulting from stone passage through the common bile duct. However, limited data exist regarding the risk factors for significant aminotransferase elevation in common bile duct obstruction. The aim of this study was to investigate the risk factors for markedly elevated aminotransferases in patients with common bile duct stones who underwent endoscopic retrograde cholangiopancreatography (ERCP).

Methods: In this cross-sectional study, clinical and paraclinical findings were evaluated in 322 patients with common bile duct stones who underwent ERCP at Rouhani Hospital in Babol. The patients were divided into two groups: a case group comprising individuals with ALT and/or AST levels ≥ 500 IU/L, and a control group comprising individuals with ALT and/or AST levels < 500 IU/L. The two groups were compared regarding sex, presence of pain, common bile duct diameter, and gallstone size.

Findings: Of the 322 patients evaluated, 131 were assigned to the case group (ALT/AST≥ 500 IU/L) and 191 to the control group (ALT/AST< 500 IU/L). The overall mean age of the patients was 62.02±13.46 years. The frequency of common bile duct stones in the case group was 38.7%. Significant differences were observed between the case and control groups with respect to younger age (52.22±21.71), female sex, presence of pain, smaller common bile duct diameter (9.72±6.10 mm), and smaller stone size (10.33±4.37 mm) ($p<0.05$). These factors were independently associated with enzyme elevation.

Conclusion: The results of this study demonstrated that risk factors including younger age, female sex, presence of pain, common bile duct diameter, and stone size may influence the elevation of liver enzymes. These findings may assist in improving the management of patients undergoing ERCP.

Keywords: *Aspartate Aminotransferase (AST), Alanine Aminotransferase (ALT), Endoscopic Retrograde Cholangiopancreatography (ERCP), Common Bile Duct (CBD).*

Cite this article: Shokri Shirvani J, Akbari Shahabi P, Gholinia H, Behzad C. Risk Factors for Markedly Elevated Aminotransferases in Patients with Common Bile Duct Stones. *Journal of Babol University of Medical Sciences*. 2026; 28: e17.

Copyright © 2024 Babol University of Medical Sciences. Published by Babol University of Medical Sciences. This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International license (https://creativecommons.org/licenses/by-nc/4.0/). Noncommercial uses of the work are permitted, provided the original work is properly cited.

Introduction

Elevation of liver transaminases, including alanine aminotransferase (ALT) and aspartate aminotransferase (AST), has been shown to be helpful in the diagnosis of liver diseases and injuries (1, 2). Liver injury is generally divided into hepatocellular and cholestatic types. A marked increase in liver aminotransferases is most frequently observed in hepatocellular damage (1, 2). In biliary tract disorders and cholestasis, aminotransferase levels typically do not rise significantly (3), with the exception of biliary obstruction caused by stone passage through the common bile duct (4). In patients with elevated liver transaminases due to such stone passage, the severity of pain varies (2, 5). Normal ranges for ALT and AST vary according to sex, age, and geographic region and are approximately 8-40 U/L; mild transaminase elevation is defined as levels up to 250 U/L (6). The frequency of marked aminotransferase elevation in patients with choledocholithiasis has not been fully determined (7-10). Insufficient and conflicting information exists regarding the risk factors for marked aminotransferase elevation in patients with common bile duct stones. In patients with choledocholithiasis, it is essential to remove the stone from the common bile duct in order to alleviate pain and symptoms and to prevent complications such as pancreatitis and cholangitis (11-13).

Endoscopic retrograde cholangiopancreatography (ERCP) is one of the diagnostic and therapeutic tools used for common bile duct stones (14). Although ERCP was initially introduced as a diagnostic procedure, its invasive nature has transformed it into a primarily therapeutic tool in recent years (11-16). Understanding the risk factors for a significant increase in aminotransferase levels in patients with common bile duct stones may help improve the diagnostic and therapeutic management of these patients. Rouhani Hospital is one of the main referral centers in northern Iran for the treatment of biliary stones using ERCP. Given that limited information is available in this area-particularly in Iran-the aim of this study was to investigate the frequency and risk factors for markedly elevated aminotransferase in patients with common bile duct stones who underwent ERCP at Rouhani Hospital in Babol.

Methods

After approval by the Ethics Committee of Babol University of Medical Sciences (code: IR.MUBABOL.REC.1402.113), this cross-sectional study was conducted on 322 patients with common bile duct stones who underwent ERCP between 2009 and 2021. Confirmation of stone diagnosis on ERCP by a gastroenterology subspecialist was required for inclusion. Exclusion criteria included choledochoduodenal fistula, biliary tract malignancies, concomitant pancreatitis, absence of AST/ALT testing, use of hepatotoxic drugs immediately before the procedure, and liver disorders such as fatty liver and chronic hepatitis. Patient records with confirmed ERCP diagnosis of common bile duct stones were extracted from archived endoscopy reports and reviewed. After application of inclusion and exclusion criteria, eligible patients were enrolled and divided into case and control groups. Patients with ALT and/or AST levels ≥ approximately 500 U/L were assigned to the case group, and those with levels < approximately 500 U/L were assigned to the control group. The cutoff value of approximately 500 U/L was selected based on previous studies (4, 16). Data on demographic characteristics (sex and age), clinical symptoms, cholangiography findings, AST and ALT levels, pain, common bile duct diameter, stone size, and stone number were extracted from patient records and compared. Data analysis was performed using SPSS version 22. Descriptive statistics, including mean, standard deviation, and frequency, were calculated. Statistical comparisons were made using t-tests, chi-square tests, Mann-Whitney tests, and univariate and multivariate logistic regression. A p-value of less than 0.05 was considered statistically significant.

Results

This study examined 322 patients with common bile duct stones who underwent ERCP between 2009 and 2021. The mean age of the patients was 62.02±13.46 years. Among them, 197 (61.2%) were female and 125 (38.8%) were male. In 38.7% of the patients, at least one liver enzyme level was measured at approximately 500 U/L or higher. When compared to the control group, the case group was found to have significantly younger age, smaller common bile duct diameter, and smaller stone size ($p<0.05$). Although the case group had a lower mean number of stones than the control group, this difference did not reach statistical significance (Table 1).

Univariate and multivariate logistic regression analyses, using the Enter method, were performed to evaluate the predictive value of variables for case and control status. Each model included the following variables: age, female sex, common bile duct diameter, stone number, stone size, and presence of pain. The dependent variable for both analyses was assignment to the case group. For sex, the reference variable was male; for pain, the reference was its absence. In the univariate analysis, age ($p<0.001$), female sex ($p=0.022$), common bile duct diameter ($p=0.001$), stone size ($p<0.001$), and presence of pain ($p=0.044$) were significant predictors of case group membership. However, none of these variables remained statistically significant in the multivariate analysis (Table 2).

Table 1. Comparison of baseline variables between the case group and control group

Variable	Case Group (n=131)	Control Group (n=191)	p-value*
Age (years), Mean±SD	52.22±21.71	67.68±14.26	<0.001**
Sex, Number(%)			
Female	90(31.3)	107(44.0)	0.022
Male	41(68.7)	84(56.0)	
Age category, Number(%)			
<50 years	64(49.6)	20(10.5)	<0.001
≥50 years	65(50.4)	170(89.5)	
Pain, Number(%)			
No	15(15.0)	37(25.9)	0.042
Yes	85(85.0)	106(74.1)	
CBD diameter (mm), Mean±SD	9.72±6.10	15.30±7.34	<0.001**
Stone number, Mean±SD	1.55±0.87	1.61±2.04	0.163**
Stone size (mm), Mean±SD	10.33±4.37	13.44±4.19	<0.001**

*Chi-square test, **Mann-Whitney test

Table 2. Effect of baseline variables on patient mortality

Variable	Univariate Analysis				Multivariate Analysis			
	Odds Ratio	p-value	95% Confidence Interval		Odds Ratio	p-value	95% Confidence Interval	
			Lower Limit	Upper Limit			Lower Limit	Upper Limit
Age	0.953	<0.001	0.940	0.966	1.014	0.520	0.971	1.060
Sex (female)	1.723	0.022	1.080	2.749	0.355	0.239	0.063	1.992
Common bile duct diameter	0.899	<0.001	0.857	0.942	0.943	0.409	0.821	1.083
Stone count	0.982	0.868	0.792	1.218	2.636	0.065	0.940	7.388
Presence of pain	1.978	0.044	1.018	3.844	0.719	0.706	0.130	3.981

Discussion

The findings of this study demonstrated that among 322 patients with a mean age of 62.02±13.46 years, more than 60% were female. Furthermore, in the evaluation of ERCP findings, the mean common bile duct diameter among patients was approximately 14 mm. Patients had more than one stone on average, with a mean stone size of about 13 mm. Our study revealed that the frequency of elevated aminotransferases (ALT and AST) above approximately 500 U/L was 7.38%. Our results are consistent with the findings of Björnsson et al., who reported that approximately 8% of patients with choledocholithiasis had significantly elevated ALT and smaller bile duct diameters (4). Nathwani et al. noted in their study that nearly 6.9% of patients with common bile duct stones had a marked elevation (above approximately 1000 U/L) and 18% had a moderate elevation (between approximately 500-1000 U/L) in hepatic aminotransferase levels (17). Another study by Bangaru et al. reported the frequency of elevated liver enzymes in patients with common bile duct stones as 6.1% (18). In a study conducted by Huh et al., it was noted that among 882 patients examined, 4.3% had aminotransferase levels above approximately 400 U/L (9).

In the study by Yurgaky-Sarmiento et al., a 10 to 20-fold increase in liver enzyme levels was reported in 8.3% of patients (18), which is close to our reported figures. The discrepancies between our findings and those of some other studies may be attributed to differences in patient populations, time periods, and overall study design. In examining the associations between the case and control groups, our study demonstrated that younger age, female sex, presence of pain, smaller common bile duct diameter, and smaller stone size were significantly comparable between the case and control groups, suggesting that these factors may be significantly associated with ALT and/or AST levels ≥ approximately 500 U/L in patients who underwent ERCP due to common bile duct stones. These factors independently influenced the elevation of hepatic aminotransferases. This study showed that for each one-unit increase in age, the odds ratio for elevation of these enzymes decreased by 4.7% in patients who underwent ERCP due to common bile duct stones. A similar protective relationship was observed with respect to increased common bile duct diameter and stone size. Furthermore, we demonstrated that female sex and presence of pain increased the odds of elevated aminotransferases by 1.72-fold and 1.97-fold, respectively.

In a study conducted by Björnsson et al., it was noted that patients with ALT> 500 U/L were significantly younger than other patients with common bile duct stones. The bile duct diameter in these patients, as well as in those with high transaminase levels (ALT>1000 U/L), was significantly smaller (2). Jeon et al. also reported that patients with higher levels were younger and had narrower CBDs (19). Therefore, it can be concluded that the presence of a stone in a narrower bile duct may cause a sudden increase in bile duct pressure and a greater elevation of transaminases. The diameter of the extrahepatic bile duct increases with age (18). The results of the present study, which demonstrate the relationship between age and common bile duct diameter with high levels of hepatic aminotransferases, are similar to and confirm these findings. Bangaru et al. also reported in another study that patients with high aminotransferases had smaller bile duct diameters and were more likely to have a history of previous cholecystectomy (17). This supports the theories regarding the mechanism of aminotransferase elevation in choledocholithiasis, suggesting that increased intra-bile duct pressure due to sudden obstruction by a bile duct stone leads to backflow of bile into the liver, which causes hepatocellular injury. Consequently, this releases hepatic cellular enzymes into the bloodstream (18, 19).

In a study conducted by Huh et al., it was noted that the case group, similar to our study, consisted predominantly of younger patients who experienced more abdominal pain and had a narrower CBD compared to the control group. They also, consistent with our findings, found no significant association between the case and control groups with respect to the number of stones (9). In a study by Zare et al., it was reported that CBD diameter remained the sole independent risk factor in the model for predicting

common bile duct stones. They noted that elevated liver enzyme levels did not play a primary role in CBD diagnosis, and ERCP for suspected CBD stones was not indicated based solely on elevated liver enzymes, even with normal ultrasound findings (20). This finding is consistent with our study, which demonstrated that increased CBD diameter independently had an inverse relationship with stone formation; however, this relationship was not significant when considered alongside other variables including age and other ERCP findings. Future studies should be considered to better elucidate the associations among these factors. Therefore, knowledge of these risk factors can provide a strategy for better triage of patients presenting with these risk factors, either to expedite or to delay the ERCP procedure. By following patients with common bile duct stones who have undergone ERCP and identifying risk factors influencing the elevation of liver enzymes in these patients, preventive measures can be implemented in the management of patients being considered for ERCP due to stones.

Furthermore, the results of this study demonstrate effective risk factors for performing and adjusting the timing of ERCP management in patients at the bedside. A limitation of our study is that it was conducted at a single center. Additionally, not considering medication and opium use as potential confounding factors may also be among our limitations. Therefore, generalizing these findings to the entire population requires a larger, multicenter study. Furthermore, the status of underlying diseases, which may act as confounding factors affecting the results, was not examined. Another important consideration is the patient follow-up status, which, due to missing data, may have influenced the results. Accordingly, it is recommended that a study with a larger sample size be conducted taking these factors into account to better evaluate the effect of these variables.

Acknowledgment

The authors wish to thank the Vice-Chancellor for Research and Technology of Babol University of Medical Sciences, the Medical Records Department of Ayatollah Rouhani Hospital, and colleagues at the campus.

References

1.Giannini EG, Testa R, Savarino V. Liver enzyme alteration: a guide for clinicians. CMAJ. 2005;172(3):367-79.
2.Björnsson ES, Bergmann OM, Björnsson HK, Kvaran RB, Olafsson S. Incidence, presentation, and outcomes in patients with drug-induced liver injury in the general population of Iceland. Gastroenterology. 2013;144(7):1419-25, e1-3.
3.Pratt D, Kaplan M. Evaluation of the liver (Laboratory tests). In: Diseases of the Liver, 1st ed. Schiff ER, Sorrell MF, Maddrey WC, editors. Philadelphia: Lippincott-Raven; 1999. p.100-6.
4.Björnsson HK, Björnsson ES. A significant proportion of patients with choledocholithiasis have markedly elevated alanine aminotransferase. Scand J Gastroenterol. 2019;54(9):1155-9.
5.Sharara AI, Mansour NM, El-Hakam M, Ghaith O, El Halabi M. Duration of pain is correlated with elevation in liver function tests in patients with symptomatic choledocholithiasis. Clin Gastroenterol Hepatol. 2010;8(12):1077-82.
6.Ramachandran P, Perisetti A, Gajendran M, Chakraborti A, Narh JT, Goyal H. Increased Serum Aminotransferase Activity and Clinical Outcomes in Coronavirus Disease 2019. J Clin Exp Hepatol. 2020;10(6):533-9.
7.Isogai M, Hachisuka K, Yamaguchi A, Nakano S. Etiology and pathogenesis of marked elevation of serum transaminase in patients with acute gallstone disease. HPB Surg. 1991;4(2):95-105.
8.Nathwani RA, Kumar SR, Reynolds TB, Kaplowitz N. Marked elevation in serum transaminases: an atypical presentation of choledocholithiasis. Am J Gastroenterol. 2005;100(2):295-8.
9.Huh CW, Jang SI, Lim BJ, Kim HW, Kim JK, Park JS, et al. Clinicopathological features of choledocholithiasis patients with high aminotransferase levels without cholangitis: Prospective comparative study. Medicine (Baltimore). 2016;95(42):e5176.
10.Tetangco EP, Shah N, Arshad HM, Raddawi H. Markedly Elevated Liver Enzymes in Choledocholithiasis in the absence of Hepatocellular Disease: Case Series and Literature Review. J Investig Med High Impact Case Rep. 2016;4(2):2324709616651092.
11.Kim JY, Lee HS, Chung MJ, Park JY, Park SW, Song SY, et al. Bleeding Complications and Clinical Safety of Endoscopic Retrograde Cholangiopancreatography in Patients with Liver Cirrhosis. Yonsei Med J. 2019;60(5):440-5.
12.Buxbaum JL, Abbas Fehmi SM, Sultan S, Fishman DS, Qumseya BJ, Cortessis VK, et al. ASGE guideline on the role of endoscopy in the evaluation and management of choledocholithiasis. Gastrointest Endosc. 2019;89(6):1075-105.e15.
13.Dahale AS, Puri AS, Sachdeva S, Srivastava S, Kumar A. Endoscopic Retrograde Cholangiopancreaticography in Children: A Single-center Experience From Northern India. Indian Pediatr. 2019;56(3):196-8.
14.Meseeha M, Goosenberg E, Attia M. Endoscopic Retrograde Cholangiopancreatography. [Updated 2025 Oct 5]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2026. Available from: https://www.ncbi.nlm.nih.gov/books/NBK493160/
15.Halász A, Pécsi D, Farkas N, Izbéki F, Gajdán L, Fejes R, et al. Outcomes and timing of endoscopic retrograde cholangiopancreatography for acute biliary pancreatitis. Dig Liver Dis. 2019;51(9):1281-6.
16.Fortson WC, Tedesco FJ, Starnes EC, Shaw CT. Marked elevation of serum transaminase activity associated with extrahepatic biliary tract disease. J Clin Gastroenterol. 1985;7(6):502-5.
17.Bangaru S, Thiele D, Sreenarasimhaiah J, Agrawal D. Severe Elevation of Liver Tests in Choledocholithiasis: An Uncommon Occurrence With Important Clinical Implications. J Clin Gastroenterol. 2017;51(8):728-33.
18.Yurgaky-Sarmiento J, Otero-Regino W, Gómez-Zuleta M. Elevated transaminases: a new tool for the diagnosis of choledocholithiasis. A case control study. Un estudio de casos y controles. Rev Colomb Gastroenterol. 2020;35(3):319-28.

19.Jeon WJ, Han JH, Seo JC, Park SM, Chae HB, Youn SJ. [Clinical features of patients with choledocholithiasis showing high levels of aminotransferases]. Korean J Gastroenterol. 2006;47(3):213-7. [Korean]
20.Zare M, Kargar S, Akhondi M, Mirshamsi MH. Role of liver function enzymes in diagnosis of choledocholithiasis in biliary colic patients. Acta Med Iran. 2011;49(10):663-6.