Assessment of biliary tree anatomy and its clinical implications

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Abstract. Anatomical variations in the intrahepatic duct (IHD) and cystic duct (CD) are common, and their accurate identification is essential for preoperative planning. The present study aimed to assess the prevalence of biliary ductal variations using magnetic resonance cholangiopancreatography (MRCP), to explore the association between IHD and CD and to evaluate potential associations with common biliary disorders. In the present retrospective study, a total of 259 patients, who were referred for MRCP due to various biliary-related clinical indications, including biliary stones, cholecystitis and obstructive jaundice, between January 2019 and December 2023, were included. Variations of the IHD and CD were classified based on imaging findings. Associations with biliary stones, cholecystitis and obstructive jaundice were assessed using the χ^2 test and univariable and multivariable logistic regression analyses. IHD variations were identified in 38.6% of cases, which was most commonly attributed to a trifurcation pattern (22%), followed by drainage of the right posterior duct into the common hepatic duct (8.5%) or the left hepatic duct (7.7%). CD variations were observed in 36.7% of cases, which were most commonly medial anterior (17.8%) or posterior (18.9%) spiral insertions. A significant association was found between IHD and CD variations (P=0.010). CD variations were also associated with a higher prevalence of biliary stones (P=0.023) and cholecystitis (P=0.048). In multivariable analysis, IHD variation [adjusted odds ratio (aOR)=1.95; 95% confidence interval (CI), 1.14-3.35; P=0.015] and biliary stones (aOR=1.79; 95% CI, 1.03-3.12; P=0.041) were independent predictors of CD anatomical variants. In conclusion, anatomical variations of the IHD and CD were common and strongly associated. Recognizing these variants could be essential for preoperative planning and aid in anticipating complications, particularly given their association with stone formation and cholecystitis.

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Abbreviations: MRCP, magnetic resonance cholangiopancreato graphy; IHD, intrahepatic duct; EHD, extrahepatic duct; CD, cystic duct; RAD, right anterior duct; RPD, right posterior duct; LHD, left hepatic duct; CHD, common hepatic duct; RHD, right hepatic duct; CBD, common bile duct; KAUH, King Abdullah University Hospital; OR, odds ratio; aOR: adjusted OR; CI, confidence interval

Key words: bile duct, hepatic duct, CD, MRCP, stones

Introduction

The liver is anatomically divided into eight independent segments, each supplied by its own portal and hepatic venous systems (1). Segment I (the caudate lobe) is located between the ligamentum venosum and the inferior vena cava. The middle hepatic vein separates the remaining portion of the liver into right and left lobes. The right lobe comprises segments V, VI, VII and VIII, while the left lobe includes segments II, III and IV. The left lobe is further subdivided by the umbilical fissure and falciform ligament into lateral (segments II and III) and medial (IV, the quadrate lobe) segments (2).

The hepatobiliary tree consists of both intrahepatic ducts (IHDs) and extrahepatic ducts (EHDs). The intrahepatic biliary system is formed by the right hepatic duct (RHD) and left hepatic duct (LHD). The RHD arises from the confluence of the right posterior duct (RPD), which drains segments VI and VII, and the right anterior duct (RAD), which drains segments V and VIII. Typically, the RPD follows a relatively horizontal course, whereas the RAD is more vertically oriented. The LHD is formed by the biliary ducts of segments II, III and IV. The RHD and LHD join to form the common hepatic duct (CHD), which is then joined by the cystic duct (CD) from the gallbladder. The CD most commonly inserts into the middle third of the CHD on its right-lateral side, forming the common bile duct (CBD). The CBD empties the main pancreatic duct into the major duodenal papilla in the second part of the

duodenum (2-4). This conventional biliary anatomy is present in 55-65% of the general population worldwide (3-5).

Although anatomical variations of the IHD and CD have been well described in other populations, such as Asian, European and American, their prevalence within Middle Eastern populations, as well as their interrelationship and clinical significance with biliary conditions, such as gallstone disease, cholecystitis and obstructive jaundice, remain insufficiently explored. Importantly, previous studies (6-12) have evaluated IHD and CD variations separately, with limited data addressing their combined occurrence and impact on biliary pathology. A thorough understanding of biliary anatomy is crucial for anatomists, radiologists and surgeons, as unrecognized variations can increase the risk of postoperative complications, such as bile duct injury, biliary peritonitis, jaundice and sepsis (2,5,13-17). Therefore, the present study aimed to investigate the coexistence of IHD and CD variations and evaluate their effect on biliary pathology in a Middle Eastern population using magnetic resonance cholangiopancreatography (MRCP).

Materials and methods

Study design and setting. The present retrospective, cross-sectional, single-center, observational study included 259 patients who met the following inclusion criteria: Referral for MRCP for a biliary-related indication; adequate image quality allowing full visualization of the biliary tree; and availability of complete medical record at King Abdullah University Hospital (KAUH; Irbid, Jordan), a tertiary referral center in Northern Jordan, between January 2019 and December 2023. The mean age of the cohort was 48.2±18.0 years, and female patients comprised 44.0% of the cohort (n=114/259). KAUH is a referral and teaching hospital affiliated with Jordan University of Science and Technology, serving >3 million individuals across four governorates. The present study was approved by the Institutional Review Board of Jordan University of Science and Technology and KAUH □(approval no. 10/163/2023; Irbid, Jordan) and conducted in accordance with the principles of The Declaration of Helsinki. Exclusion criteria included poor image quality, insufficient visualization of the IHD or CD and incomplete medical records.

Data collection. Demographic data, including age, sex and prior diagnoses associated with the biliary system, such as the presence of gallbladder or biliary tract stones, cholecystitis and obstructive jaundice, were systematically extracted from the hospital database. Patient data were accessed and extracted in stages between September 2023 and May 2024. Clinical variables were determined based on documented clinical diagnoses and imaging findings, with relevant laboratory investigations reviewed when necessary to support the diagnosis of biliary obstruction.

Imaging technique. All MRCP examinations were performed using a standardized protocol on a 1.5-T MR system (Ingenia; Philips Healthcare). The imaging parameters were as follows: Repetition time of 401 msec, echo time of 80 msec, flip angle of 90 degrees and field of view of 343x343 mm. Thick oblique coronal and axial slices of ~8 mm interval were acquired during breath-hold. Patients fasted for 6 h prior to the examination, and no intravenous or oral contrast agents were administered. The protocol included three sequences: The T2-weighted axial single-shot turbo spin-echo sequences, T2-weighted spectral attenuated inversion recovery coronal fast spin-echo sequences and 3D respiratory-triggered heavily T2-weighted MRCP sequences. Furthermore, the heavily T2-weighted thick-slab MRCP images, the axial and coronal source images from the 3D respiratory-triggered heavily T2-weighted MRCP sequences, and the maximum intensity projection images were analyzed together to identify any possible anatomic variations. All patients were scanned in the supine position. Scans with notable technical limitations, such as poor image quality or incomplete visualization of the biliary tree were excluded to maintain diagnostic accuracy.

Image analysis. Two radiology residents independently assessed MRCP images and documented the biliary tree anatomy, including the presence of anatomical variants. The collected data were classified, and cases with poor image quality were excluded. Discrepancies were resolved by consensus with a senior consultant radiologist. All evaluations were conducted using the Picture Archiving and Communication System (PACS; Synapse PACS; FUJIFILM Corporation). The type of IHD anatomy was classified according to the system described by Huang *et al* (18). Conventional anatomy (type 1) was specified as the RPD joining the posterior RAD to form the RHD, which subsequently joins the LHD to form the CHD. Anatomical variations were classified as follows: i) Type 2, when there was a common confluence of the RPD, RAD and LHD (trifurcation); ii) type 3a, when the RPD drained into the LHD; iii) type 3b, when the RPD drained into the CHD; and iv) type 4, when other variants of the IHD were identified and sequentially numbered. Among these, a single case in which two LHDs drained into the CHD was recorded (Fig. 1A). The CD insertion into the CHD was defined based on its circumferential association with conventional anatomy as type 1, where the CD was inserted into the CHD through the right-lateral aspect. Anatomical variations were classified as follows: i) Type 2, when the CD coursed a distinctive anterior spiral pattern to the CHD, thus leading to its insertion into the left medial side of the CHD; and ii) type 3, when the CD coursed a distinctive posterior spiral pattern to the CHD, eventually resulting into its insertion into the left medial side of the CHD (Fig. 1B).

Statistical analysis. All statistical analyses were performed using Stata 16.0 (StataCorp LP). Continuous variables, such as age, are presented as the mean ± SD and were compared across anatomical groups using one-way ANOVA. Categorical variables, presented as numbers and percentages, including sex, ductal variants, lithiasis, cholecystitis and obstructive jaundice, were compared using Fisher's exact test. Univariable logistic regression analyses were carried out to identify factors associated with IHD variations and uncommon CD variations. Candidate variables were selected *a priori* based on demographic relevance, anatomical plausibility, clinical significance and availability within the retrospective MRCP dataset. Age and sex were retained as core demographic covariates. Additional variables included the corresponding

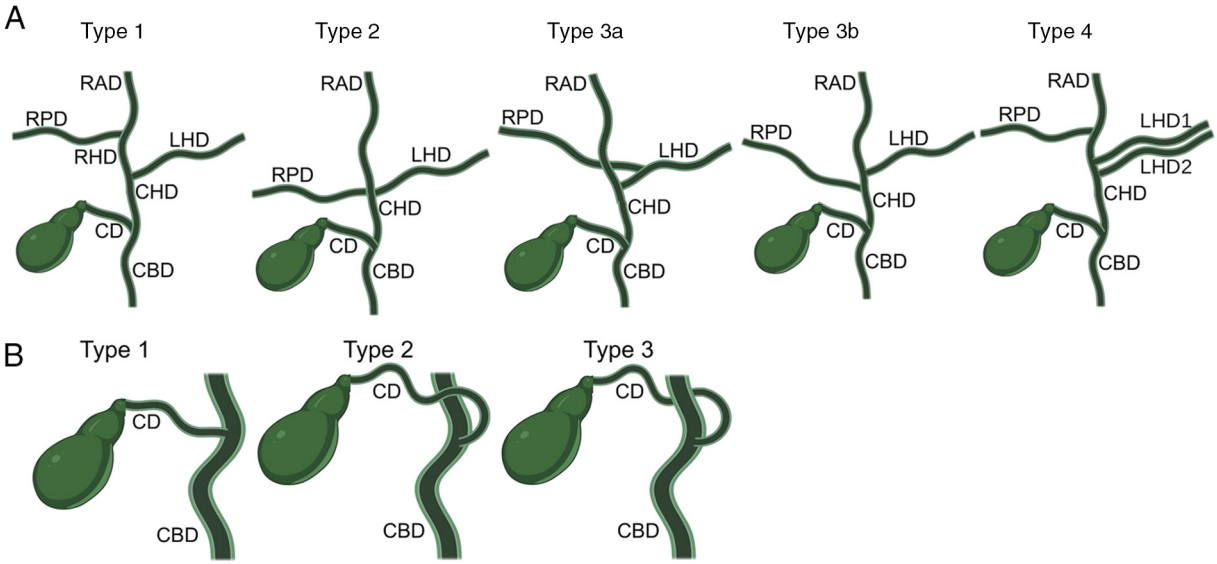

Figure 1. Schematic illustration of IHD and CD anatomical variations. (A) IHD anatomical patterns: i) Type 1, conventional anatomy, in which the RHD is formed by the confluence of the RAD and RPD, and then joins the LHD to form the CHD; ii) type 2, trifurcation pattern including the RAD, RPD and LHD; iii) type 3a, the RPD drains into the LHD; iv) type 3b, the RPD drains into the CHD; and v) type 4, presence of two LHDs draining into the CHD. (B) CD anatomical patterns: i) Type 1, lateral insertion into the CHD; ii) type 2, anterior spiral course with medial insertion into the CHD; and iii) type 3, posterior spiral course with medial insertion into the CHD. IHD, intrahepatic duct; CD, cystic duct; RAD, right anterior duct; RPD, right posterior duct; RHD, right hepatic duct; LHD, left hepatic duct; CHD, common hepatic duct; CBD, common bile duct. Created with BioRender (https://www.biorender.com/).

ductal anatomical pattern, the composite 'any biliary stone', cholecystitis and obstructive jaundice due to their clinical and anatomical relevance. Effect estimates were reported as odds ratios (ORs) and adjusted odds ratios (aORs) with 95% confidence intervals (CIs). aORs were estimated using multivariable logistic regression models adjusted for age, sex, the corresponding ductal anatomical variation, any biliary stone, cholecystitis and obstructive jaundice. Site-specific stone variables were excluded to avoid structural collinearity with the composite variable 'any biliary stone', which was retained as the primary indicator of biliary lithiasis. Model adequacy was verified using the Hosmer-Lemeshow test, and a two-sided $P<0.05$ was considered to indicate a statistically significant difference.

Results

Branching patterns of the IHD. Conventional IHD anatomy (type 1) was observed in 61.4% of cases, whereas anatomical variants were recorded in 38.6% of cases (type 2=22.0%, type 3a=7.7%, type 3b=8.5% and type 4=0.4%; Fig. 2). The differences in the study variables across IHD categories are summarized in Table I. Neither mean age nor sex distribution differed significantly across IHD categories. By contrast, CD anatomy was notably associated with the IHD pattern ($P<0.05$). CD variants were only identified in 29.6% of type 1 cases, with ~50.0% of cases presenting with type 2 (49.1%) and type 3a (55.0%) configurations. Furthermore, anterior-spiral CD insertion (CD type 2) was more common in IHD type 2 (28.1%), whereas posterior-spiral insertion (CD type 3) predominated in IHD type 3a (40.0%) ($P<0.05$ based on comparison across all CD variation types; Table I), thus indicating concordant developmental variation between IHD and EHD. Biliary stone disease was present in 40.9% of patients but was not associated with IHD pattern or other clinical variables (all $P>0.05$). Specifically, age ($P=0.900$), sex ($P=0.199$), cystic duct stones ($P=0.201$), CBD stones ($P=0.283$), gallbladder stones ($P=0.120$), any biliary stone ($P=0.052$), cholecystitis ($P=0.568$) and obstructive jaundice ($P=0.174$) did not differ significantly across IHD categories (Table I). Univariable and multivariable logistic regression analyses identifying factors associated with IHD variations are listed in Table II. CD variation was the strongest predictor, doubling the odds of harboring an IHD variant in univariable analysis (OR=2.20; 95% CI, 1.31-3.70; $P=0.003$) and remained significant after adjustment for age, sex, any biliary stone, cholecystitis and obstructive jaundice (aOR=1.95; 95% CI, 1.13-3.35; $P=0.016$). Consistently, the presence of any biliary stone in the gallbladder, CD or CBD was also independently associated with a ~2-fold increase in the odds of an IHD variant (OR=1.97; 95% CI, 1.18-3.28; $P=0.009$; aOR=2.00; 95% CI, 1.16-3.46; $P=0.013$). Age, sex, individual stone locations, cholecystitis and obstructive jaundice were not significantly associated (all $P>0.05$). Individual stone locations were not included in the multivariable model due to collinearity with the composite variable 'any biliary stone'.

Anatomical variations of CD insertion into the CBD. Conventional CD right-lateral insertion (type 1) was observed in 63.3% (n=164) of all cases (Fig. 2A), whereas CD variants were identified in 36.7%, including anterior spiral (type 2, 17.8%) and posterior spiral patterns (type 3, 18.9%) (Fig. 3). As shown in Table III, age did not differ significantly across CD patterns ($P=0.680$), and although female patients were less common among spiral variants, this difference did not reach statistical significance ($P=0.077$). Furthermore, a significant association between the IHD and EHD anatomy was evident. Particularly, IHD variants were present in approximately one-third of patients with conventional right-lateral CD

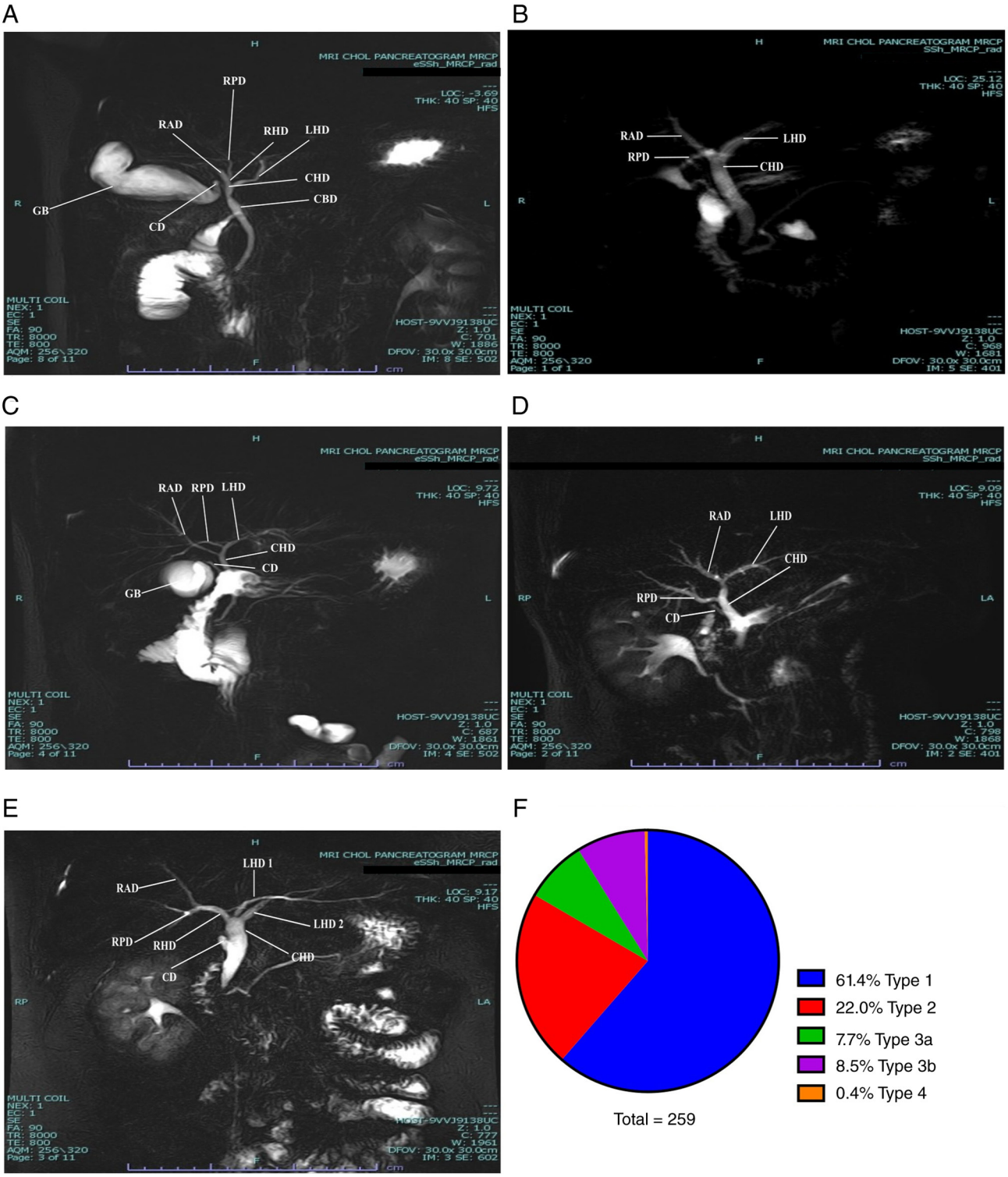

Figure 2. Representative magnetic resonance cholangiopancreatography images showing IHD anatomical variation patterns. (A) Type 1, the RAD and RPD form the RHD, which joins the LHD to form the CHD. Furthermore, the CD inserts laterally into the CHD (type 1 CD). (B) Type 2, trifurcation pattern involving the RAD, RPD and LHD. (C) Type 3a, the RPD drains into the LHD. (D) Type 3b, the RPD drains into the CHD. (E) Type 4, presence of two LHDs draining into the CHD. (F) Distribution of IHD types (n=259). IHD, intrahepatic duct; RAD, right anterior duct; RPD, right posterior duct; RHD, right hepatic duct; LHD, left hepatic duct; CHD, common hepatic duct; CD, cystic duct; GB, gallbladder; H, head; F, feet; R, right; L, left; RP, right posterior; LA, left anterior.

insertion (type 1, 31.7%), compared with roughly half of patients with anterior (type 2, 47.8%) or posterior (type 3, 53.1%) spiral variants (P=0.010). Consistently, CD pathology followed the same hierarchy, with posterior spiral CD variants showing the highest prevalence of CD stones (P=0.047). However, it should be noted that the vast majority of patients were negative for CD stones (98.5%; 255/259), and the observed P-value should be interpreted with caution given its borderline significance. The composite variable 'any biliary stone' increased step-wise from 34.8% in type 1 to 47.8% in type 2 and 55.1% in type 3

Table I. Differences in the study variables across intrahepatic duct types.

Variable	Total (n=259)	Type 1 (n=159; 61.4%)	Type 2 (n=57; 22.0%)	Type 3a (n=20; 7.7%)	Type 3b (n=22; 8.5%)	Type 4 (n=1; 0.4%)	P-value
Age, years	48.2±18.0	48.2±18.4	50.0±19.2	41.0±13.9	49.4±13.5	60.0±0.0	0.900
Sex, n (%)							0.199
Female	114 (44.0)	76 (47.8)	18 (31.6)	10 (50.0)	10 (45.5)	0 (0.0)	
Male	145 (56.0)	83 (52.2)	39 (68.4)	10 (50.0)	12 (54.5)	1 (100.0)	
CD variation, n (%)							0.019
No	164 (63.3)	112 (70.4)	29 (50.9)	9 (45.0)	13 (59.1)	1 (100.0)	
Yes	95 (36.7)	47 (29.6)	28 (49.1)	11 (55.0)	9 (40.9)	0 (0.0)	
CD variation type, n (%)							0.031
Type 1	164 (63.3)	112 (70.4)	29 (50.9)	9 (45.0)	13 (59.1)	1 (100.0)	
Type 2	46 (17.8)	24 (15.1)	16 (28.1)	3 (15.0)	3 (13.6)	0 (0.0)	
Type 3	49 (18.9)	23 (14.5)	12 (21.0)	8 (40.0)	6 (27.3)	0 (0.0)	
CD stones, n (%)							0.201
No	255 (98.5)	157 (98.7)	57 (100.0)	19 (95.0)	21 (95.5)	1 (100.0)	
Yes	4 (1.5)	2 (1.3)	0 (0.0)	1 (5.0)	1 (4.5)	0 (0.0)	
CBD stones, n (%)							0.283
No	225 (86.9)	143 (89.9)	45 (78.9)	17 (85.0)	19 (86.4)	1 (100.0)	
Yes	34 (13.1)	16 (10.1)	12 (21.1)	3 (15.0)	3 (13.6)	0 (0.0)	
Gallbladder stones, n (%)							0.120
No	168 (64.9)	110 (69.2)	30 (52.6)	13 (65.0)	15 (68.2)	0 (0.0)	
Yes	91 (35.1)	49 (30.8)	27 (47.4)	7 (35.0)	7 (31.8)	1 (100.0)	
Any biliary stone, n (%)							0.052
No	153 (59.1)	104 (65.4)	26 (45.6)	11 (55.0)	12 (54.5)	0 (0.0)	
Yes	106 (40.9)	55 (34.6)	31 (54.4)	9 (45.0)	10 (45.5)	1 (100.0)	
Cholecystitis, n (%)							0.568
No	253 (97.7)	156 (98.1)	55 (96.5)	19 (95.0)	22 (100.0)	1 (100.0)	
Yes	6 (2.3)	3 (1.9)	2 (3.5)	1 (5.0)	0 (0.0)	0 (0.0)	
Obstructive jaundice, n (%)							0.174
No	138 (53.3)	83 (52.2)	26 (45.6)	12 (60.0)	16 (72.7)	1 (100.0)	
Yes	121 (46.7)	76 (47.8)	31 (54.4)	8 (40.0)	6 (27.3)	0 (0.0)	

CD, cystic duct; CBD, common bile duct.

Table II. Factors associated with the presence of IHD variation (IHD types 2, 3a, 3b and 4).

	Univariable regression		Multivariable regression	
Variable	OR (95% CI)	P-value	aOR (95% CI)	P-value
Age	1.00 (0.99, 1.01)	0.980	1.00 (0.98, 1.01)	0.688
Female (vs. male)	0.67 (0.40, 1.11)	0.123	0.67 (0.39, 1.14)	0.142
CD variation (present vs. absent)	2.20 (1.31, 3.70)	0.003	1.95 (1.13, 3.35)	0.016
CD stones[a] (present vs. absent)	1.60 (0.22, 11.56)	0.640	-	-
CBD stones[a] (present vs. absent)	1.96 (0.95, 4.06)	0.069	-	-
Gallbladder stones[a] (present vs. absent)	1.63 (0.97, 2.74)	0.067	-	-
Any biliary stone (present vs. absent)	1.97 (1.18, 3.28)	0.009	2.00 (1.16, 3.46)	0.013
Cholecystitis (present vs. absent)	1.61 (0.32, 8.13)	0.565	0.85 (0.15, 4.89)	0.860
Obstructive jaundice (present vs. absent)	0.89 (0.54, 1.48)	0.70	0.73 (0.42, 1.24)	0.242

[a]Site-specific stone variables were excluded from the multivariable model owing to collinearity with the composite stone variable. CD, cystic duct; CBD, common bile duct; IHD, intrahepatic duct; OR, odds ratio; aOR: adjusted OR; CI, confidence interval.

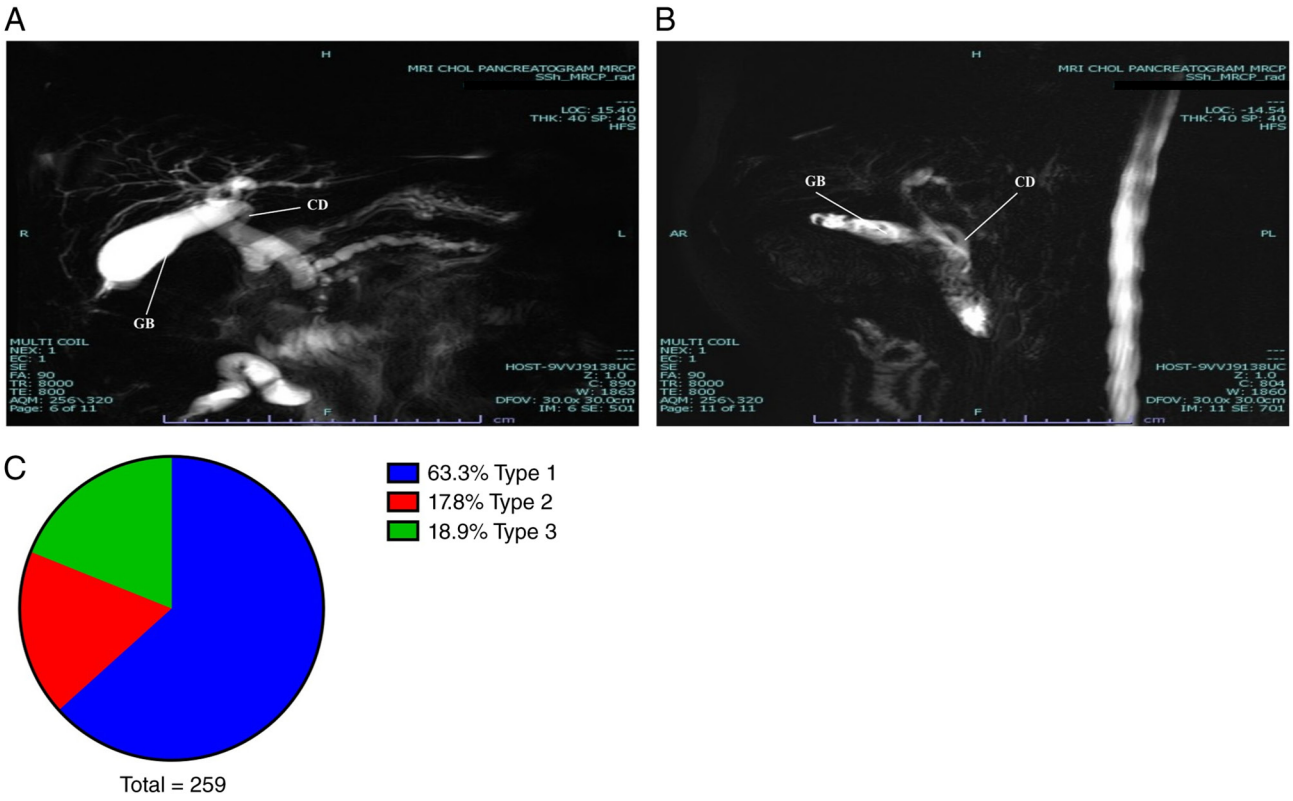

Figure 3. Representative magnetic resonance cholangiopancreatography images showing CD anatomical variation patterns. (A) Type 2, anterior spiral course with medial insertion into the CHD. (B) Type 3, posterior spiral course with medial insertion into the CHD. (C) Distribution of CD anatomical types (n=259). CD, cystic duct; CHD, common hepatic bile duct; GB, gallbladder; H, head; F, feet; R, right; L, left; AR, anterior right; PL, posterior left.

(P=0.022). A similar trend was found for cholecystitis (0.6 vs. 4.4 vs. 6.1%; P=0.039). However, it should be noted that the vast majority of patients were negative for cholecystitis (97.7%; 253/259), and these findings should therefore be interpreted with caution. By contrast, CBD stones and obstructive jaundice were not significantly associated with CD orientation (P=0.898 and P=0.179, respectively). These results suggested that spiral (medial) CD variants were associated with both IHD variations and a higher risk of lithiasis and cholecystitis. Univariable and multivariable logistic regression analyses were performed to identify factors associated with the presence of uncommon CD variants (spiral insertions; types 2 and 3). As shown in Table IV, IHD variation was the strongest independent variable associated with CD variants (OR=2.20; 95% CI, 1.31-3.70; P=0.003), and remained significant after adjustment for age, sex, any biliary stone, cholecystitis and

Table III. Differences in the study variables across CD types.

Variable	Total (n=259)	Type 1 (n=164; 63.3%)	Type 2 (n=46; 17.8%)	Type 3 (n=49; 18.9%)	P-value
Age, years	48.2±18.0	47.9±17.3	48.4±16.4	49.0±21.6	0.680
Sex, n (%)					0.077
Female	114 (44.0)	80 (48.8)	14 (30.4)	20 (40.8)	
Male	145 (56.0)	84 (51.2)	32 (69.6)	29 (59.2)	
IHD variation, n (%)					0.010
No	159 (61.4)	112 (68.3)	24 (52.2)	23 (46.9)	
Yes	100 (38.6)	52 (31.7)	22 (47.8)	26 (53.1)	
IHD variation type, n (%)					0.031
Type 1	159 (61.4)	112 (68.3)	24 (52.2)	23 (46.9)	
Type 2	57 (22.0)	29 (17.7)	16 (34.8)	12 (24.5)	
Type 3a	20 (7.7)	9 (5.5)	3 (6.5)	8 (16.3)	
Type 3b	22 (8.5)	13 (7.9)	3 (6.5)	6 (12.3)	
Type 4	1 (0.4)	1 (0.6)	0 (0.0)	0 (0.0)	
CD stones, n (%)					0.047
No	255 (98.5)	163 (99.4)	46 (100.0)	46 (93.9)	
Yes	4 (1.5)	1 (0.6)	0 (0.0)	3 (6.1)	
CBD stones, n (%)					0.898
No	225 (86.9)	142 (86.6)	41 (89.1)	42 (85.7)	
Yes	34 (13.1)	22 (13.4)	5 (10.9)	7 (14.3)	
Gallbladder stones, n (%)					0.066
No	168 (64.9)	115 (70.1)	26 (56.5)	27 (55.1)	
Yes	91 (35.1)	49 (29.9)	20 (43.5)	22 (44.9)	
Any biliary stone, n (%)					0.022
No	153 (59.1)	107 (65.2)	24 (52.2)	22 (44.9)	
Yes	106 (40.9)	57 (34.8)	22 (47.8)	27 (55.1)	
Cholecystitis, n (%)					0.039
No	253 (97.7)	163 (99.4)	44 (95.7)	46 (93.9)	
Yes	6 (2.3)	1 (0.6)	2 (4.3)	3 (6.1)	
Obstructive jaundice, n (%)					0.179
No	138 (53.3)	90 (54.9)	19 (41.3)	29 (59.2)	
Yes	121 (46.7)	74 (45.1)	27 (58.7)	20 (40.8)	

CD, cystic duct; CBD, common bile duct; IHD, intrahepatic duct.

obstructive jaundice (aOR=1.95; 95 % CI, 1.14-3.35; P=0.015). Similarly, the presence of lithiasis was also independently associated with spiral CD variants (OR=2.00; 95% CI, 1.19-3.35; P=0.008; aOR=1.79; 95% CI, 1.03-3.12; P=0.041). In addition, female sex showed a modest protective effect against uncommon CD variants in the univariable analysis (OR=0.59; 95% CI, 0.35-0.98; P=0.043). However, this association was not retained after adjustment (aOR=0.60; 95% CI, 0.35-1.04; P=0.070). Cholecystitis exhibited a univariable association, although the wide 95% CI (1.04-78.71) and borderline P-value (P=0.046) indicate that this result should be interpreted with caution (OR=9.06; 95% CI, 1.04-78.71; P=0.046), but was attenuated in the multivariable model (aOR=8.31; 95% CI, 0.88-78.02; P=0.064). Age, site-specific stone location and obstructive jaundice were not significantly associated with spiral CD insertions (all P>0.05). Notably, gallbladder stone showed a significant association in the univariable analysis (OR=1.86; 95% CI, 1.10-3.14; P=0.021); however, site-specific stone variables were excluded from the multivariable model due to collinearity with the composite variable 'any biliary stone'.

Discussion

The present study investigated the prevalence and clinical associations of biliary ductal anatomical variations in a Jordanian population using MRCP. Conventional IHD anatomy (type 1) was observed in 61.4% of cases, whereas 38.6% exhibited variant branching patterns. Consistently, the right-lateral CD insertion (type 1) was present in 63.3% of patients, while medial insertions accounted for 36.7%. A

Table IV. Factors associated with the presence of uncommon CD variation (CD variation types 2 and 3).

	Univariable regression		Multivariable regression	
Variable	OR (95% CI)	P-value	aOR (95% CI)	P-value
Age	1 (0.99, 1.02)	0.723	1 (0.99, 1.02)	0.817
Female (vs. male)	0.59 (0.35, 0.98)	0.043	0.6 (0.35, 1.04)	0.070
IHD variation (present vs. absent)	2.2 (1.31, 3.7)	0.003	1.95 (1.14, 3.35)	0.015
CD stones[a] (present vs. absent)	5.32 (0.54, 51.84)	0.151	-	-
CBD stones[a] (present vs. absent)	0.93 (0.44, 1.98)	0.857	-	-
Gallbladder stones[a] (present vs. absent)	1.86 (1.1, 3.14)	0.021	-	-
Any biliary stone (present vs. absent)	2 (1.19, 3.35)	0.008	1.79 (1.03, 3.12)	0.041
Cholecystitis (present vs. absent)	9.06 (1.04, 78.71)	0.046	8.31 (0.88, 78.02)	0.064
Obstructive jaundice (present vs. absent)	1.19 (0.72, 1.98)	0.499	1.06 (0.62, 1.83)	0.832

[a]Site-specific stone variables were excluded from the multivariable model owing to collinearity with the composite stone variable. CD, cystic duct; CBD, common bile duct; IHD, intrahepatic duct; OR, odds ratio; aOR: adjusted OR; CI, confidence interval.

significant association between IHD and CD variations was identified, thus indicating a potentially coordinated developmental association. Compared with the majority of previous studies (6-12) that had evaluated these anatomical systems independently, in the present study a combined analysis of IHD and CD variations was performed, which demonstrated a statistically significant interrelationship. Furthermore, variant CD insertions were associated with a higher prevalence of biliary lithiasis and cholecystitis, highlighting their clinical relevance. These findings extended prior work, such as that by Renzulli *et al* (19) by confirming the coexistence of IHD and CD variations and further highlighting the clinical relevance of CD variations. Whereas Renzulli *et al* focused primarily on IHD anatomy with EHD as a secondary aim, the present study specifically characterized CD insertion variants as the primary outcome and their independent clinical predictors using multivariable analysis. In addition, the present study is the first to evaluate these associations in a Middle Eastern population, directly addressing the limitation acknowledged by Renzulli *et al* regarding the generalizability of their findings beyond an almost exclusively European series from a single Italian center. A comprehensive understanding of biliary anatomy is essential for accurate preoperative planning and for minimizing complications during hepatobiliary procedures (2,20). It has been reported that anatomical variations can increase the risk of bile duct injury during laparoscopic cholecystectomy, with an incidence of 0.5-1.7% as reported across multiple international studies (14,15,21), thus resulting in severe complications, including jaundice, biliary peritonitis, sepsis and secondary biliary cirrhosis (16,17). Certain IHD variations carry important surgical implications. The trifurcation pattern (type 2), in which the RPD, RAD and LHD share a common confluence point, is considered a contraindication for safe right hepatectomy in living donor liver transplantation, as it necessitates additional biliary anastomoses in the recipient, increasing the risk of postoperative biliary complications (22). The type 3a IHD variant, in which the RPD drains into the LHD, are important, as they can complicate liver transplantation and increase donor risk (22). Unrecognized type 3a anatomy during left hepatectomy can also result in bile leakage, biliary stasis, recurrent infections or cirrhosis due to RPD transection or ligation (9). A previous study demonstrated that in percutaneous transhepatic drainage, obstruction of the LHD could lead to cholestasis in the right posterior lobe (7). Therefore, particular variants, such as types 2 and 3a, are considered relative contraindications for liver donation in some centers (22,23).

Several classification systems have described IHD variations (24). In the present study, the Huang classification (18) was adopted due to its simplicity and clinical applicability. The prevalence of conventional anatomy varies across populations, with higher rates reported in Asian populations (~65%) compared with European and American ones (~60%) (25). Consistent with prior studies (7,9,18,19,22,24,26-28), in the present study no significant sex-based differences were observed, although certain reports suggested a higher prevalence of IHD variants among women (25,29).

The proportion of conventional IHD anatomy in the current study (61.4%) lied within the range reported in the literature (41.0-87.0%) (5-9,11,12,19,20,25-27,29-42). The most common variation was type 2 trifurcation (22.0%), although its prevalence varied widely in previous studies (3.0-44.0%) (5,19,25,27,30,37,40,42). Types 3a and 3b occurred in 7.7 and 8.5% of cases, respectively, which were also within previously reported ranges (2.2-27.8% and 1.5-10%, respectively) (5-9,11,12,19,20,25-27,29-42). A rare variant involving draining of two separate LHDs into the CHD was identified in one case (0.4%), which was consistent with prior reports of low prevalence of this variant (0.2-2.4%) (7,20,27,30,40). Other rare variations, such as drainage of the RPD or RHD into the CD, or the presence of accessory hepatic ducts, which have been reported in previous studies (5-8,20,26,27,30-32,34, 37,40), were not observed in the present study.

A key finding of the present study was the strong association between CD insertion patterns and IHD variations, an observation that has been previously noted (19). For example, type 2 CD insertion was most commonly associated with type 2 IHD, while type 3 CD frequently co-occurred with type

3a IHD. Preoperative identification of EHD anatomy could therefore help anticipate corresponding variations in IHD. The aforementioned association could likely reflect a shared embryologic origin from the hepatic diverticulum, where the pars hepatica forms the IHD, while the pars cystica gives rise to the CD, CBD and gallbladder (43). Disruptions in this developmental process could account for the concurrent occurrence of variations in both systems (19,43,44).

By contrast, CD anatomy lacks a standardized classification system (10). Existing studies have described CD variants using descriptive anatomical classifications and imaging-based approaches that categorize variations by insertion site, course and morphology (6,10,11,23,45,46). These descriptive and imaging-based strategies collectively highlight the heterogeneity in the characterization of CD variations. Therefore, the present study employed a simplified MRCP-based classification system focusing on insertion patterns and course, as these features are consistently identifiable and clinically relevant. The distinction between conventional lateral insertion and medial spiral insertions represents a well-reported and clinically important pattern across MRCP-based studies (6,10,11,46-48). In contrast to existing systems that variably emphasize insertion level, duct length or complex morphological configurations, the present classification focused on parameters consistently visualized on MRCP and directly applicable to surgical planning and radiological reporting. Specifically, classification according to CD insertion pattern and course enables consistent identification and reporting of anatomical variants on MRCP. For example, recognition of anterior or posterior spiral CD insertion can be explicitly communicated in radiological reports and considered during preoperative assessment, thereby improving awareness of atypical biliary anatomy and facilitating surgical planning for hepatobiliary procedures. Accordingly, the current classification was intended as a pragmatic and reproducible reporting framework aligned with routine MRCP practice, rather than as a substitute for more comprehensive anatomical classification systems.

CD variations are considered to arise from embryologic malrotation during duodenal development, resulting in anterior or posterior spiral courses around the CHD (49). In the present study, conventional CD anatomy was observed in 63.3% of cases, slightly lower than rates reported in previous studies (76.1-89%) (6,10,11,46). These variants can increase the risk of bile duct injury and intraoperative bile leakage during laparoscopic cholecystectomy (50).

Although IHD variations were not directly associated with specific clinical conditions, they frequently co-occurred with atypical CD insertions. Spiral CD variants, particularly posterior types, were more commonly associated with biliary stones and inflammation, potentially due to impaired bile flow and stasis (10,51). Multivariable analysis revealed that both IHD variations and biliary stones independently predicted CD variants, while CD variants were strongly associated with IHD variations. These findings supported the interrelationship between intrahepatic and extrahepatic biliary anatomy and their combined contribution to disease pathology.

The observed association between CD variations, biliary lithiasis and cholecystitis further supports the clinical importance of recognizing biliary anatomical variants during preoperative evaluation. From a practical perspective, current evidence supports a selective rather than routine application of MRCP prior to cholecystectomy. The American Society for Gastrointestinal Endoscopy guidelines (52) advocate a risk-stratified approach, categorizing patients into low-, intermediate- and high-probability groups for CBD stones. To verify the diagnosis, the American Society for Gastrointestinal Endoscopy recommends that patients with an intermediate risk (10-50%) of choledocholithiasis should undergo endoscopic ultrasound or MRCP (53). A subsequent study further supported this strategy, suggesting that intermediate-risk classification could guide the use of additional imaging, including MRCP or endoscopic ultrasound, rather than performing routine imaging in all patients (53). Furthermore, the American Society for Gastrointestinal Endoscopy guidelines have been associated with a reduced number of unnecessary diagnostic endoscopic retrograde cholangiopancreatographies, thus minimizing procedure-related complications (52,53). Particularly, identification of CD variations or complex biliary anatomy is clinically important, as it can alert the surgeon to an increased risk of misidentification and warrant a more cautious dissection strategy. When anatomical variation is identified or suspected, a cautious operative approach is essential (54), involving careful dissection to achieve the critical view of safety; a method of target identification requiring: Clearance of the hepatocystic triangle of fat and fibrous tissue, separation of the lower third of the gallbladder from the cystic plate, and confirmation that only the CD and cystic artery remain attached to the gallbladder before clipping and division (54). When these criteria cannot be safely met, bail-out strategies such as subtotal fenestrating cholecystectomy should be employed, and intraoperative imaging considered when anatomy remains unclear, as part of a broader strategy to improve operative safety (54). Given that EHD and IHD variants may coexist, identification of any variation should prompt a systematic search for additional ductal variations (19). In this context, preoperative identification of complex biliary anatomy should be incorporated into patient counseling, informed consent and operative planning for possible intraoperative imaging or endoscopic procedures.

The present study has several limitations. Firstly, its retrospective, cross-sectional design limits inference of causal relationships between biliary anatomical variations and associated clinical conditions. In addition, several potential confounders, including body mass index, metabolic syndrome, diabetes, dyslipidemia and medication history, were not consistently available in the present retrospective imaging-based study and therefore could not be included in the multivariable analyses. Consequently, the aORs should be interpreted as associations adjusted for the available demographic, anatomical and radiological variables, rather than as fully adjusted causal estimates accounting for all metabolic or systemic clinical risk factors. Furthermore, the single-center design could limit the generalizability of the results, as the study population was derived from a tertiary referral center that typically manages more complex or symptomatic cases. This could introduce referral bias, potentially leading to an overrepresentation of patients with biliary pathology compared with the general population. Consistent with this possibility, the relatively high prevalence of biliary

stones (40.9%) likely reflects selection bias, given that MRCP is more commonly performed in patients with suspected biliary disease rather than in asymptomatic individuals. Consequently, the observed associations between anatomical variations and biliary pathology could be overestimated and should therefore be interpreted with caution. Additionally, patients referred for MRCP may not accurately reflect the true distribution of biliary anatomical variations in the general population. Therefore, future multicenter prospective studies, including more representative populations, are needed to externally validate these findings. Lastly, although MRCP is a reliable, non-invasive imaging tool for evaluation of the biliary system, its spatial resolution can occasionally fail to identify rare anatomical variations.

In conclusion, IHD and CD variations are common and strongly associated, supporting a shared developmental origin. Their identification is of clinical importance for surgical planning and risk stratification, particularly given the association of CD variants with biliary lithiasis and inflammation. Identification of a variation in one component should prompt careful evaluation for concurrent variations in the other. Patients with such variations may also benefit from closer monitoring due to their potentially increased susceptibility to stone formation and cholecystitis.

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Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

WM and NO contributed to the conceptualization and design of the study. WM, NO, AA and HAJ wrote the manuscript. Image acquisition and analysis were performed by AM, AAD, HAJ and NO. Data analysis and interpretation were carried out by WM, AA and SM. WM and NO confirm the authenticity of all the raw data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The present study was approved by the Institutional Review Board of Jordan University of Science and Technology and KAUH (approval no. 10/163/2023). The study adhered to all applicable national regulations and institutional policies regarding human research and was conducted in accordance with the ethical principles outlined in The Declaration of Helsinki. The Institutional Review Board waived the requirement for informed consent due to the retrospective design of the study, as all personal identifiers were removed to ensure that no patient could be identified, either directly or indirectly.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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