Magnetic resonance cholangiopancreatography identification of pancreaticobiliary maljunction in the colombian pediatric population

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ABSTRACT

Overview. Pancreaticobiliary maljunction (PBM) is a congenital malformation characterized by a long common pancreaticobiliary channel which causes sphincter of Oddi malfunction. In children, it is typically diagnosed using magnetic resonance cholangiopancreatography (MRCP). It is associated with congenital biliary dilatation, pancreatitis, and gallbladder and bile duct tumors at adulthood. Studies in the western population are rare. Given its morbidity rate, it should be searched for in the western pediatric population. The objective of this study was to look for and identify the presence of pancreaticobiliary maljunction through MRCP in pediatric patients with biliary or pancreatic disease, as well as to find out other associated factors.

Methods. MRCP was used to measure common channel length, pancreatic duct length, and bile duct diameter in 41 pediatric patients with biliary or pancreatic disease.

Results. The common channel could only be measured in 17.6% of cases, 50% of which were >8 mm long. All patients were female and had congenital biliary dilatation. No age-related differences were found in terms of bile duct length.

Conclusions. PBM is present in the western pediatric population, but prevalence and morbidity are unknown. Larger studies are required to identify morbidity and mortality, as well as prevalence among patients.

KEY WORDS: Common channel; Pancreaticobiliary maljunction; Magnetic resonance cholangiopancreatography; Congenital biliary dilatation; Common bile duct; Pancreatic duct.

UNIÓN BILIOPANCREÁTICA ANÓMALA POR COLANGIORRESONANCIA EN POBLACIÓN PEDIÁTRICA COLOMBIANA

RESUMEN

Objetivo. La unión biliopancreática anómala (UBPA) es una malformación congénita caracterizada por un canal común pancreatobiliar largo que impide el adecuado funcionamiento del esfínter de Oddi. Su diagnóstico en niños se realiza comúnmente mediante colangiopancreatografía por resonancia magnética (CPRM). Se asocia a dilatación biliar congénita, pancreatitis y tumores de la vesícula y la vía biliar en la edad adulta. Los estudios en población occidental son escasos; debido a su morbilidad resulta de relevancia la búsqueda en población pediátrica occidental. Este estudio pretende buscar e identificar la presencia de unión biliopancreática anómala mediante CPRM de pacientes pediátricos con enfermedad de la vía biliar o pancreática, al igual que identificar otros factores asociados.

Métodos. Se midió por CPRM la longitud del canal común, el conducto pancreático y el diámetro de la vía biliar de 41 pacientes pediátricos con patología biliar o pancreática.

Resultados. El canal común solo pudo ser medido en el 17,6% de los casos, de los cuales el 50% tuvo una longitud >8 mm, siendo todos ellos pacientes femeninos con dilatación biliar congénita; no se encontraron diferencias en la longitud de la vía biliar relacionado con la edad.

Conclusiones. La UBPA es una malformación que se encuentra presente en población pediátrica occidental con prevalencia y morbilidad desconocida; se requieren estudios a mayor escala para identificar morbimortalidad y prevalencia de pacientes con esta malformación.

PALABRAS CLAVE: Canal común; Unión biliopancreática anómala; Colangiopancreatografía por resonancia magnética; Dilatación biliar congénita; Conducto biliar común; Conducto pancreático.

INTRODUCTION

Pancreaticobiliary maljunction (PBM) is a congenital abnormality where the pancreatic duct and the common bile duct junction is located outside the duodenal wall, thus forming a long common channel[(1)]. There is no standard value regarding common channel length. According

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Work partially presented at the 21st Colombian Congress of Pediatric Surgery held in September 2018. International Congress, Bogotá – Ágora Convention Center. Type of product: poster.

Date of submission: January 2020 *Date of acceptance:* June 2020

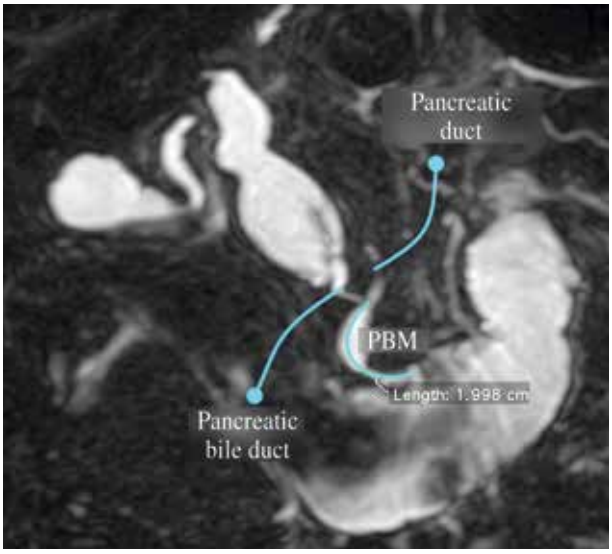

Figure 1. Magnetic resonance cholangiopancreatography demonstrating pancreaticobiliary maljunction (PBM) and common bile duct dilatation.

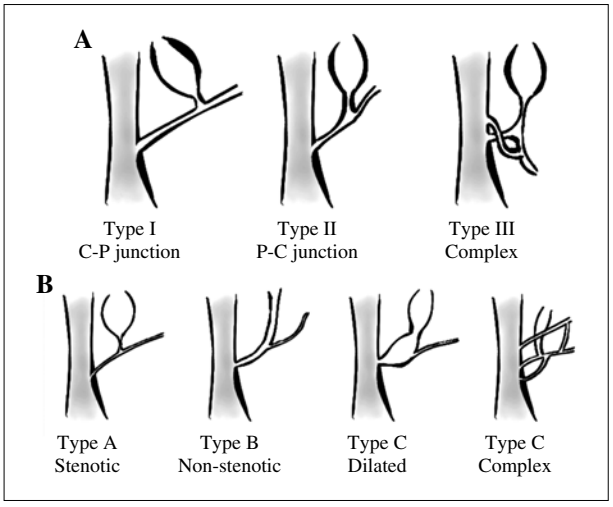

Figure 2. A) Komi classification. B) Classification by the Diagnostic Criteria Committee of the Japanese Study Group on PBM.

to the literature, it can be as long as 8 mm, 12 mm, or even 15 mm. However, the junction is considered normal when the common channel is ≤8 mm long at magnetic resonance cholangiopancreatography (MRCP) imaging (Fig. 1)[2].

The objective of this study was to look for PBM in western pediatric patients using MRCP, and to determine if it is present and whether there are associated factors, laying the foundations for subsequent larger studies. A literature review was carried out to establish some basic concepts and definitions for PBM active search.

Located at the distal extremity of the common bile duct and the pancreatic duct, the sphincter of Oddi regulates biliary and pancreatic juice outflow to the duodenum[1,3]. However, in PBM cases, it does not play its full role at the junction of both ducts, which means there is biliary and pancreatic juice reflux in both directions[4].

PBM prevalence in Japan is approximately 0.1%[5]. It is relatively unknown in the western world, but some studies demonstrate pathological findings similar to those noted in the eastern population[6]. It is associated with pancreatitis (acute, recurrent, or chronic) in 9% of adults and 28-43.6% of children. Bile duct cancer occurs 15-20 years earlier in PBM patients than in non-PBM patients, approximately between 50 and 65 years of age. Bile duct cancer incidence in pediatric patients (under 15 years old) remains unknown. It has not been established whether there is concomitant pancreatic cancer predisposition or not[1,5].

The most frequent PBM symptoms include abdominal pain and jaundice. Clinically speaking, it can progress to cholangitis and pancreatitis. >8,000 IU/L intra-biliary amylase levels and >8 mm common channel lengths have been associated with a positive predictive value and a >90% specificity[1].

There are two PBM classifications:

1. Komi classification (Fig. 2a)[1,6]:
   - Type I or A (type C-P, bile duct, or right angle): the bile duct joins the pancreatic duct.
   - Type II or B (P-C, pancreatic duct, or acute angle): the pancreatic duct joins the bile duct.
   - Type III or C (complex): a complex junction of the pancreaticobiliary duct system occurs.
2. Classification by the Diagnostic Criteria Committee of the Japanese Study Group on PBM from 2015 (Fig. 2b)[7]:
   - Type A (stenotic): the stenotic distal segment of the common bile duct joins the common channel.
   - Type B (non-stenotic): the non-stenotic distal segment of the common bile duct joins the common channel, and local common channel dilatation cannot be seen.
   - Type C (dilated channel): the stenotic segment of the common bile duct joins the common channel, which is dilated.
   - Type D (complex): a complex junction of the pancreaticobiliary duct system occurs. PBM is associated with annular pancreas, pancreas divisum, or other complex duct systems.

PBM can be associated with congenital biliary dilatation (CBD), a rare malformation of the biliary system characterized by a cystic or fusiform dilatation of the common bile duct with or without intra-hepatic biliary dilatation. Acquired or secondary bile duct dilatation, which is caused by gallstone- or malignity-associated obstruction, is strictly excluded. Congenital biliary dilatation is included in Todani classification, according to which PBM can be a

Table 1. Indications for MRCP request.

	Number of patients
Suspected CBD	10 (29.4%)
Pancreatitis	10 (29.4%)
Cholelithiasis	5 (14.7%)
Jaundice	5 (14.7%)
Hepatopathy	3 (8.8%)
Suspected pancreatic fistula	1 (2.9%)
Total	34 (100%)

CBD: Congenital biliary dilatation.

Todani type I CBD (except for type Ib) and a Todani type IV-A CBD (>85% of patients)[3,6,8].

Adult patients with PBM and CBD have higher gallstone incidence in the biliary tract (17.9%), primarily bilirubinate gallstones. They are associated with pancreatitis in 10.5-56% of cases in adults, and 23% of cases in children[9]. PBM and CBD association is believed to be related to cholestasis, infection, and cancer development (21.6%). The presence of PBM without CBD increases cholelithiasis (27.3%) and bile duct cancer (42.4%) incidence, and prognosis is worse[1,5].

PBM should be distinguished from high confluence of pancreaticobiliary ducts (HCPBD), which is defined as a long common channel (≥6 mm long), with the sphincter of Oddi playing a partial role at the pancreaticobiliary junction[1,3]. In HCPBD, biliary amylase levels are lower than in PBM, with lower gallbladder cancer incidence probably because bi-directional reflux secondary to sphincter of Oddi's partial role at the junction is lower.

Cholecystectomy and extrahepatic bile duct resection followed by bilioenterostomy with wide anastomosis to ensure free biliary drainage is the treatment of choice for PBM with biliary dilatation. Prophylactic cholecystectomy is recommended to prevent gallbladder cancer in patients with PBM without biliary dilatation[3,4]. According to the Japanese clinical practice guidelines on PBM, symptomatic neonates and infants should undergo surgery immediately. If they are asymptomatic, surgery can be elective at 3-6 months of age[1].

Early postoperative complications include suture rupture, resection surface bleeding, acute pancreatitis, pancreatic fistula, gastrointestinal bleeding, and ileus. Late postoperative complications include cholangitis, intrahepatic lithiasis, biliary tract residual cancer, pancreatic gallstones, and pancreatitis. Gallstones in the remnant bile ducts following biliary bypass have also been described[10]. After biliary bypass for CBD, bile duct cancer incidence is 0.7-5.4%[9].

Table 2. Mean magnetic resonance cholangiopancreatography measures.

	Range	*Not measurable*	*Mean*
Common channel length	3-12 mm	28 (82.4%)	9.7 mm
Widest bile duct diameter	1.6-44 mm	1 (2.9%)	7.8 mm
Pancreatic duct diameter	1.1-11 mm	13 (38.2%)	2.3 mm

MATERIALS AND METHODS

An observational, descriptive, retrospective study was carried out from February 2017 to April 2018. Clinical histories and MRCPs of 41 patients under 18 years of age with biliary or pancreatic pathology admitted at Bogotá's La Misericordia Pediatric Hospital Foundation were reviewed. Patients with pancreaticobiliary surgery or endoscopic retrograde cholangiopancreatography (ERCP) history prior to magnetic resonance cholangiopancreatography were excluded. PBM diagnostic thresholds were >8 mm common channel and ≥6 mm HCPBD, measured by pediatric radiology experts. In addition, widest bile duct diameter and total length, pancreatic duct diameter, subsequent surgical procedure, and indications for MRCP request were assessed.

The study was approved by the hospital's ethics committee.

RESULTS

Of the 41 pediatric patients undergoing MRCP, 5 were excluded as a result of bile duct surgical history, and 2 due to imaging technical issues which prevented them from being assessed. Of the remaining 34 MRCPs, 20 (59%) were performed in girls, and 14 (41%) were carried out in children with a mean age of 8.9 years (range: 4 months-17 years).

Pancreatitis and suspected bile duct congenital dilatation were the most frequent indications for MRCP request in our study patients (Table 1).

Regarding MRCP analyzed measures, common channel mean ± standard deviation was 9.7 ± 5.9 mm (range: 3-12 mm). In addition, widest bile duct diameter was 7.8 ± 8.3 mm (range: 1.6-44 mm), and pancreatic duct diameter was 2.3 ± 2.1 mm (range: 1.1-11 mm). No common channel was identified in 82.4% of images. On the other hand, mean widest bile duct diameter was increased by the presence of patients with CBD, which is far from values reported as normal in the literature (Table 2).

Of the total of patients, there was one patient with HCPBD (6.5 mm) without CBD, and three (8.8%) with

Table 3. PBM patient characteristics.

Case	*Sex*	*Age (months)*	*Common channel length (mm)*	*Widest bile duct diameter (mm)*	*Pancreatic duct diameter (mm)*
1	F	24	18	13	1.5
2	F	9	12	8.9	1.7
3	F	48	14	21	1.3

>8mm common channel and CBD, one of whom also had pancreatitis. Of the patients diagnosed with PBM, they were all female (F) and aged ≤4 years old. Bile duct diameter was wider than the mean of the study population, and pancreatic duct diameter was ≥1.3 mm. No association between age, pancreatic duct diameter, and bile duct length was found. All patients underwent extrahepatic bile duct resection, bilioenterostomy, and cholecystectomy without complications (Table 3).

No PBM patient follow-up could be performed as a result of socioeconomic problems in patients' families and healthcare system issues.

DISCUSSION

Although PBM studies have been mostly conducted in the eastern population, this pathology is present in our environment, as demonstrated by this study. However, prevalence is unknown. In the study population, symptoms were found from lactation, and it was associated with congenital biliary dilatation (CBD) in 100% of cases. Most patients were female.

Regarding associated pathologies, the main conditions diagnosed in this study were pancreatitis and congenital biliary dilatation. In PBM, duodenal papilla sphincter (sphincter of Oddi) muscles are morphologically identical to those of the normal papilla sphincter and surround the common channel underneath the pancreaticobiliary junction. However, they do not play any role at the junction as a result of the common channel being abnormally long. Therefore, pancreatic juice and biliary flow accumulate and get mixed, while bidirectional regurgitation of pancreaticobiliary-biliopancreatic reflux occurs (Fig. 3), thus predisposing patients to various biliary and pancreatic conditions such as biliary tract cancer, cholangitis, and pancreatitis[1].

Pressure is greater at the pancreatic duct than at the common bile duct, thus generating pancreaticobiliary reflux and subsequent inflammation, biliary tract mucosa regeneration, and increase in cell-cycle turnover. This chronic stimulation of biliary epithelial cells sparks off genetic mutation processes, activating oncogenes and de-activating tumor suppressor genes, and subsequently inducing hyperplasia, dysplasia, and carcinogenesis[1,2].

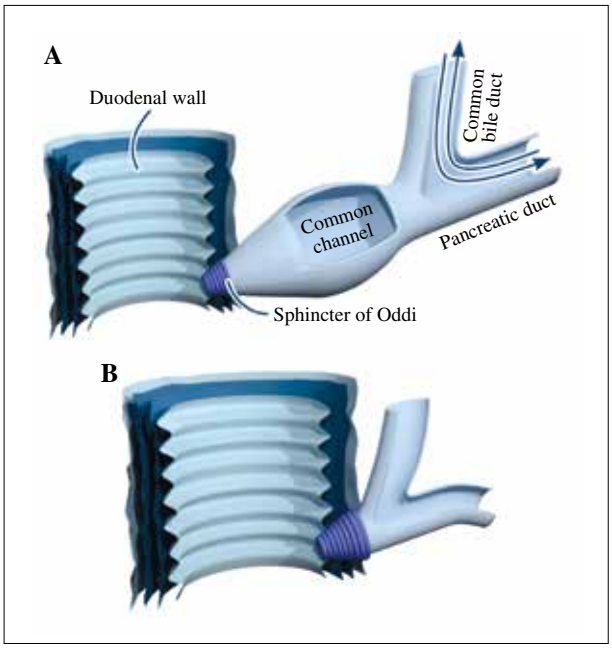

Figure 3. A) Schematic representation of PBM and bidirectional reflux. B) Normal anatomy.

This hyperplasia-dysplasia-carcinoma sequence is considered the underlying predominant mechanism of bile duct cancer[11].

Pancreatitis and pancreatic juice retention causes amylase levels to grow. Biliary retention increases direct bilirubin levels and brings about intermittent jaundice. Juice retention boosts internal pressure at the pancreatic duct and the biliary tract, causing abdominal pain and biliary enzyme increase as a result of obstruction[9].

Endoscopic retrograde cholangiopancreatography (ERCP) is PBM gold standard diagnostic technique. It involves a certain risk of complications such as bleeding and pancreatitis, which means its use should be carefully considered[1]. In pediatrics, ERCP visualization rates of PBM in bile duct cystic dilatation are quite high, ranging from 50% to 90.5%[4]. ERCP therapy has been demonstrated to significantly reduce high hepatic enzyme levels and bilirubin levels, as well as abdominal pain frequency. ERCP can be regarded as a transition tool to stabilize PBM

patients prior to definitive surgery. However, given that it is an invasive method, other diagnostic imaging techniques are preferred in the pediatric population[12].

Magnetic resonance cholangiopancreatography (MRCP) is a diagnostic alternative to ERCP. It is a non-invasive method which allows PBM to be diagnosed. However, measuring the common channel is not always feasible, either because it is too narrow or because CBD prevents the junction with the pancreatic duct from being assessed[13]. In addition, in cholangitis patients[14], it decreases imaging quality as a result of motion artifact[1,3]. This technique involves certain limitations in children – it requires sedation or anesthesia, it is expensive, it has limited availability, and it is associated with long exploration times and imaging interpretation subjectivity as a result of being operator-dependent. Nevertheless, this technique allows ducts as narrow as 1 mm in diameter to be visualized. It has also been demonstrated to provide additional findings not seen in ERCP, with which it has a concordance of 81%[15].

MRCP allows for a detailed visualization of CBD and PBM, with detection rates between 82% and 100%[6,16]. Diagnostic accuracy can be increased with tridimensional MRCP or dynamic MRCP with secretin stimulation[8,17].

This study could not establish imaging detection sensitivity and specificity as it was not compared with other studies. However, it did allow cases to be detected, which makes it a viable alternative in the active search of PBM. In our environment, MRCP and ERCP could not be compared with one another given that ERCP is little available.

Percutaneous transhepatic cholangiography (PTC) and intraoperative cholangiography (IOC) are invasive diagnostic methods associated with higher surgical and anesthetic risks. Similarly to cholangiography and ERCP, they can cause the bile duct to slightly dilate as a result of intraductal pressure increase[18].

Ultrasound imaging can be used to detect gallbladder wall thickening and congenital biliary dilatation even prenatally, when the bile duct dilates[1,9]. Additionally, it allows pancreatic duct dilatation (1-6 years: >1.5 mm; 7-12 years: >1.9 mm; 13-18 years: >2.2 mm) and other features to be visualized for pancreatitis diagnostic purposes[19]. This research found that pancreatic duct diameter can be assessed using MRCP. Nevertheless, there was no correlation between pancreatic duct diameter, pancreatitis, and PBM.

Larger studies are required in the western population to adequately determine MRCP performance in PBM diagnosis and look for findings potentially correlating pancreatitis with other radiological discoveries.

CONCLUSIONS

In the Latin American literature, there are few studies assessing PBM prevalence in the pediatric and adult population, and PBM is not actively looked for in radiological imaging. However, this study found PBM is present in our environment, and as reported by various publications, it is associated with congenital biliary dilatation and pancreatitis.

Therefore, an active MRCP search of common channel abnormal length and PBM associated parameters, such as those previously described, is recommended. It should be highlighted that this study has certain limitations which prevent results from being statistically significant and hamper MRCP performance assessment. However, it can lay the foundations for subsequent larger studies on PBM incidence and complications in the pediatric population, which will potentially complement the findings from this research.

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