Title

Complications of Endoscopic Retrograde Cholangiopancreatography in Pediatric Patients; A Systematic Literature Review and Meta-Analysis.

Authors

Usatin, Danielle
Fernandes, Melissa
Allen, Isabel E
et al.

Publication Date

2016-12-01

DOI

10.1016/j.jpeds.2016.08.046

Peer reviewed

HHS Public Access

Author manuscript

J Pediatr. Author manuscript; available in PMC 2017 December 01.

Published in final edited form as:

J Pediatr. 2016 December ; 179: 160–165.e3. doi:10.1016/j.jpeds.2016.08.046.

Complications of Endoscopic Retrograde Cholangiopancreatography in Pediatric Patients; A Systematic Literature Review and Meta-Analysis

Danielle Usatin, MD[1], **Melissa Fernandes, MD**[1], **Isabel E. Allen, PhD**[2], **Emily R. Perito, MD**[1,2], **James Ostroff, MD**[3], and **Melvin B. Heyman, MD**[1]

[1]Department of Pediatrics, University of California, San Francisco

[2]Department of Epidemiology and Biostatistics, University of California, San Francisco

[3]Department of Medicine, University of California, San Francisco

Abstract

Objectives—To systematically review risks and summarize reported complication rates associated with performance of ERCP in children over the past two decades.

Study design—A systematic literature search of MEDLINE, Embase, and Web of Science from Jan 1995 to Jan 2016 was conducted for observational studies published in English. Studies reporting ERCP complications in patients <21 years without history of liver transplant or cholecystectomy were included. A summary estimate of the proportion of children who experienced complications following ERCP was derived using a random effects meta-analysis.

Results—Thirty-two studies involving 2612 children and 3566 procedures were included. Subjects' ages ranged from 3 days to 21 years. Procedures were performed for biliary (54%), pancreatic (38%), and other (8%) indications. 56% of ERCPs were interventional. The pooled complication rate was 6% (95% CI: 4%– 8%). Procedural complications included post-ERCP pancreatitis (166, 4.7%), bleeding (22, 0.6%) and infections (27, 0.8%). The pooled estimate of post-ERCP pancreatitis was 3% (95%CI 0.02–0.05), and other complications were 1% (95%CI: 0.02–0.05). In neonatal cholestasis subgroup the pooled complication rate was 3% (95% CI: 0.01–0.07). Adult and pediatric gastroenterologists and surgeons performed the ERCPs. Available data limited the ability to report differences between pediatric-trained and other endoscopists.

Conclusions—Complications associated with pediatric ERCP range widely in severity and are reported inconsistently. Our review suggests 6% of pediatric ERCPs have complications. Further studies using systematic and standardized methodologies are needed to determine the frequency and risk factors for ERCP related complications.

Corresponding Author: Melvin B. Heyman, MD, 550 16th Street, 5th Floor, UCSF Box 0136, San Francisco, CA 94143, P: 415-476-5892, F:415-353-2472, mel.heyman@ucsf.edu.

The authors declare no conflicts of interest.

Keywords

ERCP; children; pancreas; hepatobiliary; neonatal cholestasis; endoscopist; safety

Endoscopic retrograde cholangiopancreatography (ERCP) is a specialized procedure that combines gastrointestinal endoscopy and fluoroscopy for diagnostic and therapeutic management of disorders of the pancreas and biliary tract. The procedure has been widely applied in adults for over 40 years. The first reported procedure in a child was in 1976 by Waye using an adult-sized duodenoscope (1). Smaller diameter duodenoscopes developed in the 1980s and 1990s led to expanding application of ERCP in children. ERCP allows less invasive access to the biliary tree and pancreatic duct than surgery or transhepatic procedures.

Although the utility and feasibility of ERCP in pediatrics has been demonstrated in case reports and series, concerns about safety remain. In 2000, the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) subcommittee on Endoscopy Procedures published a narrative review of data on indications, technical considerations, risks and complications of ERCP in children (2). Since that time, the number of ERCPs performed on children has increased(3). In addition, many additional studies on ERCP in pediatric patients have made this procedure appear routine. However, complication rates appear to vary between case series, potentially dependent on multiple factors including patient selection, operator, and underlying disease factors (4–7).

By conducting a systematic literature review, we examined complication rates for pediatric patients undergoing ERCP and compared complication rates by patient characteristics, endoscopist training, and center type.

METHODS

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) I statement was used to identify and collate studies (8). We systematically searched MEDLINE/PubMed, Ovid Embase, and Web of Science for full text articles in which subjects <21 years of age underwent ERCP. Complications were reported as an outcome. We used the following search phrase ((technical AND (success OR successes OR outcome OR outcomes) OR quality assurance OR patient safety OR complications OR treatment outcomes OR intraoperative complications OR postoperative complications) AND ((pediatric OR child OR children OR childhood OR adolescent OR teen OR infant OR toddler)) AND (“Cholangiopancreatography, Endoscopic Retrograde“ OR Endoscopic Retrograde Cholangiopancreatography OR ERCP)) to identify articles.

To find articles that may have been missed during the literature search, reference lists of candidate articles were also reviewed. The search was limited to English language texts from January 1995-January 2016. The final search was completed on February 10, 2016. The limitation to studies published since January 1995 was to avoid overlap with a previously published review(2).

Study Selection Criteria

Two independent reviewers screened all articles for methodological validity and relevance prior to inclusion in the review. Any disagreements between the two reviewers were resolved through discussion with a third reviewer. Our selection criteria were specified in advance and included the following: (1) published in English in a peer-reviewed journal; (2) available in full text; (3) included youth <21 years of age, excluding children who had undergone previous liver transplant or other hepatobiliary surgical procedure (eg, for choledochal cyst, cholecystectomy, for cholelithiasis); (4) observational study designs; (5) studies that examined the number and type of complications after an ERCP. If multiple articles were available from a single center, the most recently published article or the article containing the most comprehensive detail of study characteristics was selected for review.

Article Review and Data Extraction

Data were extracted from papers included in the review using a standardized data extraction tool created for this study in REDCap electronic data capture tools hosted at University of California, San Francisco(9). REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies, providing 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources. The data were extracted by two reviewers (D.U., M.F.). Once completed, any disagreements were arbitrated by a third reviewer (M.H.).

The data extracted included details about the study population, study methods and outcomes of significance to the review question and specific objectives. The study center type, endoscopist type, anesthetic type, patient characteristics, indications and findings of ERCP, and percent of procedures which were interventional were collected. If not specifically stated in the manuscript, we attempted to determine the training background of the endoscopist by searching the internet to identify current position within hospital system in adult or pediatric gastroenterology program. This systematic review is registered on Prospero (http://www.crd.york.ac.uk/PROSPERO :CRD42016038065).

Data synthesis

Studies were categorized based on the author, year of publication, subjects' age, procedure indication, and interventional or diagnostic procedure type. The complication prevalence for each study was summarized and compiled. Statistical analysis was performed using Microsoft Excel and STATA Version 13. Significant variations in study design and reporting amongst included publications precluded use of a standard definition for post-ERCP complications. We performed a random effects meta-analysis of the data using the Metaprop program (STATA 13) to provide a summary estimate of the proportion of children with complications following ERCP. We chose random effects to account for the variability among the studies, given that most were case reports and case series. Metaprop allowed for the inclusion of studies with complication proportions of 0 to 1(10).

In addition to the overall complication rate, secondary analyses were performed to further understand factors impacting the summary estimate. A subgroup analysis was performed on cases from American centers. Additionally, a sensitivity analysis of all studies was performed following the exclusion of three papers that were felt to be outliers. Outliers were identified based on the findings from the inclusive summary estimate. Finally, a random effects meta-analysis of the complications that excluded post-ERCP-associated pancreatitis (PEP) was performed.

Literature Search Results

The PRISMA flow diagram was used to document the literature search process (Figure 1; available at www.jpeds.com). We identified 1932 articles and imported these into Endnote software. Duplicates were removed and any remaining duplicates were manually removed, leaving 1642 articles. A thorough review of all article titles and abstracts yielded 44 articles that were reviewed in full. Subsequently, 12 articles were excluded for the following reasons: not reporting complication rates, presentation of patients counted in other included study, and/or including patients who had undergone liver transplant or cholecystectomy. Of the studies that included patients with a mixture of patients who did and did not meet our exclusion criteria (n=3), it was not possible to distinguish the complication rates. As such, the entire study was excluded. Ultimately, 32 articles were identified (4–7, 11–38).

RESULTS

All 32 included studies were retrospective cohort studies or case series reporting on ERCP related complications in pediatric patients. From these articles, data was obtained on 2612 children and adolescents, who underwent a total of 3566 ERCPS. Some children accounted for multiple procedures within the same article. The median number of patients per study was 44, with a range of 3 to 276 patients. Studies differed in their definition of post-procedure observation periods, which may have impacted what was considered an ERCP related complication. Only 14 of the 32 studies specified their follow up period (7, 11–23). The range of follow up time was 2 days to 30 months.

Fourteen of the 32 studies were conducted in the US (4–6, 13–16, 25–31). All 32 of the studies were from referral centers. Three of the studies were multicenter (14, 16, 18). We were unable to determine if the procedures were performed in stand-alone children's hospitals.

Four studies reported exclusively on 237 biliary ERCPs in infants (11, 19, 22, 35), and the rest included patients from birth to 21 years (Tables I and II; available at www.jpeds.com). Five studies did not report sex; of the remaining 27, 54% of included subjects were male (Table III; available at www.jpeds.com).

Procedure characteristics

ERCPs were done for biliary indications (54%), pancreatic indications (38%) or other indications including abdominal pain (8%). Overall, 56% of procedures were interventional, and the remainder were solely diagnostic (Table II).

Adult gastroenterology-trained endoscopists performed a majority of ERCPs reported in these studies. Only 2 of the 32 reports specifically stated that a pediatric gastroenterologist performed the endoscopy (7, 31). One report cited a general surgeon who performed the ERCPs(5). Eleven studies did not specify who performed the procedure.

ERCPs were performed under both general anesthesia and sedation in 19 studies. General anesthesia was exclusively used in 10 studies (6, 11, 16, 19, 21, 22, 30, 31, 34, 35, 38). Sedation was used exclusively in two studies(7, 12).

ERCP complications

Reported complications varied widely ranging from bleeding to post-ERCP pancreatitis (PEP) to fussiness. No deaths were reported in any of the studies as a consequence of ERCP. Five studies cited the ASGE lexicon for endoscopic adverse events by Cotton et al (39) to define complications and follow up period (6, 26, 27, 31, 36). The severity of complications was not documented in most studies. We aggregated complications into broad categories: PEP, infection, bleeding, and other (Table II).

Out of all 3566 procedures performed, 291 (8.2%) involved complications. The pooled overall complication rate was 6% (95% CI: 4%–8%) (Figure 2). Analysis revealed significant heterogeneity among the studies (I^2=80.54%, p<0.001), with three outlier studies (4, 20, 30). Kamelmaz et al was a small series and reported complications in two of the three performed procedures(4). Prasil et al reported one instance of bleeding and six episodes of PEP in 21 patients (20). Rescorla et al only included 6 subjects and was limited to patients with pancreatic trauma, of which 4 had complications (30). Removal of these three studies from the analysis resulted in the same pooled estimate of complications (6%; 95% CI: 4%–8%). PEP was reported in 166 of 3566 (4.7%) of procedures; bleeding was reported in 22 (0.6%); and infection was reported in 27 (0.8%). The pooled estimate of complications other than PEP was 1% (95% CI: 0%–3%). The pooled estimate of PEP as a complication was 3% (95% CI: 0.02–0.05).

Further subgroup analyses were performed to identify important factors contributing to the heterogeneity of the studies including pediatric trained endoscopists, US centers, and neonatal cholestasis. In the two studies performed by pediatric trained endoscopists, there were 238 procedures with an overall complication rate of 4.6%. A pooled overall complication rate for the 14 US sites was 5% (95% CI: 2%–10%). Among the four studies reporting solely on ERCP in neonatal cholestasis, the complication rate was 4.2% out of 238 procedures, with a pooled complication rate of 3% (95% CI: 0.01–0.07) (Figure 3; available at www.jpeds.com). Excluding these four neonatal studies, the pooled estimate of the complication rate for the remaining studies was 6% (95% CI: 4% – 9%).

DISCUSSION

Our analysis documents that the mean prevalence of complications after ERCP performed in children aged 0–21 years is approximately 6%. In contrast, the estimated complication rates of upper endoscopy has been reported as 2.3% (40) and of colonoscopy, 1.1% (41), in the same patient population. Post-ERCP pancreatitis was the most commonly reported

complication, and rates of other serious complications including bleeding and infection were less than 1% each. Since 2000, when the last comprehensive report on ERCP in pediatric patients was published (2), use of ERCP in pediatric patients with pancreatic and biliary disease have become increasingly prevalent(3). Numerous single center experiences with information on utility and feasibility of ERCP have been published, but to date no benchmarks for acceptable or expected complication rates exist. We report a complication rate that can be used in future ERCP research to explore factors such as the effects of subtype of procedure, patient characteristics or endoscopist training.

Our review of the literature also demonstrates the heterogeneity of previous studies. This highlights the need for a more standardized approach to complication reporting, even in small studies. A few studies cite the ASGE recommended guidelines for determining complications (39). Although these guidelines provide definitions for AEs and levels of severity they have yet to be adapted to pediatric populations. We were unable to apply standardized definitions for what constitutes a complication of ERCP; the studies reviewed report a wide variety of complication types with no specific definition or severity for any of the complications reported. This suggests that certain issues still need to be defined, for example anatomic location of complication, timing in relation to the procedure, and severity.

One unanswered question is whether the pediatric or adult endoscopist should be tasked with the procedure in pediatric patients, particularly infants and young children. Pediatric patients who require ERCP are often managed at pediatric referral centers where pediatricians, pediatric anesthesiologists, surgeons, radiologists, and pediatric intensivists coordinate care for these patients. Even though a pediatric-trained gastroenterologist might be more appropriate to perform the procedure in young patients, inadequate case volume both in training and in maintenance of skills is frequently cited as a reason for these procedures to be performed by adult-trained endoscopists (42–44). Our study is unable to answer this question, as only 2 reports of primarily pediatric trained gastroenterologists performing the ERCPs were available for inclusion in our review.

Post-ERCP pancreatitis was the most common complication reported, but classification of this is challenging. Six of the 32 studies did not report on post-ERCP pancreatitis as a complication. We cannot discern whether they had no cases, or if they considered post-procedure pain and pancreatic enzyme elevation to be expected outcomes of pancreatic duct visualization. Institutions may not routinely measure amylase or lipase levels after ERCP, even if patients experience abdominal pain. Troendle et al recently investigated factors associated with post-ERCP pancreatitis, noticing this occurred in 10.9% of ERCPs. They found pancreatic duct injection, sphincterotomy, or a history of chronic pancreatitis placed subjects at higher odds of PEP(45). Our pooled complications rate was lower than this, but documentation of complications after ERCP in the pediatric population was inconsistent in the reviewed studies, indicating the need for future prospective studies in this area.

Additional limitations of the existing literature are lack of consistency with reported follow-up times and minimal data available about the temporal relationship of complications to ERCP date. Studies varied, with some only reporting complications evident in the 1–2 days

following the procedure, and others including the full follow up time reported, occasionally longer than a year.

The intent of this review was to investigate what is known about the factors that impact the rate of complications in pediatric ERCP. However, we found that the majority of studies fail to relate complications to the other covariates of interest. For example, one might expect an increased rate of PEP with instrumentation of the pancreatic duct and/or pancreatic disease. However, few studies report complication rates by intervention type or by disease state. Furthermore, the effect of endoscopist training, sedation versus anesthesia, or indication on complications are not evaluable, as these factors are all reported separately.

Despite these limitations, our report does provide a comprehensive picture of available literature on complications after pediatric ERCP. We hope our findings, and data missing from previously reported literature that would be clinically helpful, will provide groundwork for future studies to further our knowledge in this area. Prospective data collection across multiple centers is needed to determine which patient-, facility-, and physician-factors are important to optimize the safety and efficacy of pediatric ERCP. The Pediatric ERCP Database Initiative is a multicenter international database currently collecting data on all patients undergoing ERCP under the age of 18 years (http://www.utsouthwestern.edu/research/fact/detail.html?studyid=STU%20012014–086). This information will enhance our ability to provide a reliable consent process for these procedures. Efforts should also be made to standardize our definitions of post-ERCP complications, so that information will be generalizable to all centers performing this procedure in children.

Acknowledgments

Supported by the Cystic Fibrosis Foundation (<grant number> [to D.U.]) and the National Institutes of Health (T32 DK007762 [to D.U. and M.F.] and K23 DK099253-01A1 [E.P.]).

References

1. Waye JD. Endoscopic retrograde cholangiopancreatography in the infant. Am J Gastroenterol. 1976; 65(5):461–3. [PubMed: 949055]
2. Fox VL, Werlin SL, Heyman MB. Endoscopic retrograde cholangiopancreatography in children. Subcommittee on Endoscopy and Procedures of the Patient Care Committee of the North American Society for Pediatric Gastroenterology and Nutrition. J Pediatr Gastroenterol Nutr. 2000; 30(3):335–42. [PubMed: 10749424]
3. Pant C, Sferra TJ, Barth BA, Deshpande A, Minocha A, Qureshi WA, et al. Trends in endoscopic retrograde cholangiopancreatography in children within the United States, 2000–2009. J Pediatr Gastroenterol Nutr. 2014; 59(1):57–60. [PubMed: 24509307]
4. Kamelmaz I, Elitsur Y. Pancreas divisum–the role of ERCP in children. The West Virginia medical journal. 1999; 95(1):14–6. [PubMed: 9949690]
5. Green JA, Scheeres DE, Conrad HA, Cloney DL, Schlatter MG. Pediatric ERCP in a multidisciplinary community setting – Experience with a fellowship-trained general surgeon. Surgical Endoscopy and Other Interventional Techniques. 2007; 21(12):2187–92. [PubMed: 17514391]
6. Enestvedt BK, Tofani C, Lee DY, Abraham M, Shah P, Chandrasekhara V, et al. Endoscopic retrograde cholangiopancreatography in the pediatric population is safe and efficacious. J Pediatr Gastroenterol Nutr. 2013; 57(5):649–54. [PubMed: 23760230]

7. Poddar U, Thapa BR, Bhasin DK, Prasad A, Nagi B, Singh K. Endoscopic retrograde cholangiopancreatography in the management of pancreaticobiliary disorders in children. J Gastroenterol Hepatol. 2001; 16(8):927–31. [PubMed: 11555109]
8. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS medicine. 2009; 6(7):e1000097. [PubMed: 19621072]
9. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)–a metadata-driven methodology and workflow process for providing translational research informatics support. Journal of biomedical informatics. 2009; 42(2):377–81. [PubMed: 18929686]
10. Nyaga VN, Arbyn M, Aerts M. Metaprop: a Stata command to perform meta-analysis of binomial data. Archives of public health = Archives belges de sante publique. 2014; 72(1):39. [PubMed: 25810908]
11. Aabakken L, Aagenaes I, Sanengen T, Aasen S, Emblem R, Bjornland K. Utility of ERCP in neonatal and infant cholestasis. Journal of laparoendoscopic & advanced surgical techniques Part A. 2009; 19(3):431–6. [PubMed: 19216697]
12. Agarwal J, Nageshwar Reddy D, Talukdar R, Lakhtakia S, Ramchandani M, Tandan M, et al. ERCP in the management of pancreatic diseases in children. Gastrointest Endosc. 2014; 79(2): 271–8. [PubMed: 24060520]
13. Giefer MJ, Kozarek RA. Technical outcomes and complications of pediatric ERCP. Surgical endoscopy. 2015; 29(12):3543–50. [PubMed: 25673350]
14. Hsu RK, Draganov P, Leung JW, Tarnasky PR, Yu AS, Hawes RH, et al. Therapeutic ERCP in the management of pancreatitis in children. Gastrointest Endosc. 2000; 51(4 Pt 1):396–400. [PubMed: 10744808]
15. Tagge EP, Tarnasky PR, Chandler J, Tagge DU, Smith C, Hebra A, et al. Multidisciplinary approach to the treatment of pediatric pancreaticobiliary disorders. J Pediatr Surg. 1997; 32(2): 158–64. discussion 64–5. [PubMed: 9044114]
16. Varadarajulu S, Wilcox CM, Hawes RH, Cotton PB. Technical outcomes and complications of ERCP in children. Gastrointest Endosc. 2004; 60(3):367–71. [PubMed: 15332025]
17. Li ZS, Wang W, Liao Z, Zou DW, Jin ZD, Chen J, et al. A long-term follow-up study on endoscopic management of children and adolescents with chronic pancreatitis. Am J Gastroenterol. 2010; 105(8):1884–92. [PubMed: 20216535]
18. Paris C, Bejjani J, Beaunoyer M, Ouimet A. Endoscopic retrograde cholangiopancreatography is useful and safe in children. J Pediatr Surg. 2010; 45(5):938–42. [PubMed: 20438931]
19. Petersen C, Meier PN, Schneider A, Turowski C, Pfister ED, Manns MP, et al. Endoscopic retrograde cholangiopancreaticography prior to explorative laparotomy avoids unnecessary surgery in patients suspected for biliary atresia. J Hepatol. 2009; 51(6):1055–60. [PubMed: 19726099]
20. Prasil P, Laberge JM, Barkun A, Flageole H. Endoscopic retrograde cholangiopancreatography in children: A surgeon's perspective. J Pediatr Surg. 2001; 36(5):733–5. [PubMed: 11329577]
21. Rocca R, Castellino F, Daperno M, Masoero G, Sostegni R, Ercole E, et al. Therapeutic ERCP in paediatric patients. Dig Liver Dis. 2005; 37(5):357–62. [PubMed: 15843086]
22. Shanmugam NP, Harrison PM, Devlin J, Peddu P, Knisely AS, Davenport M, et al. Selective use of endoscopic retrograde cholangiopancreatography in the diagnosis of biliary atresia in infants younger than 100 days. J Pediatr Gastroenterol Nutr. 2009; 49(4):435–41. [PubMed: 19680152]
23. Zargar SA, Javid G, Khan BA, Yattoo GN, Shah AH, Gulzar GM, et al. Endoscopic sphincterotomy in the management of bile duct stones in children. American Journal of Gastroenterology. 2003; 98(3):586–9. [PubMed: 12650791]
24. Abukhalaf A. The Role of Endoscopic Retrograde Cholangiopancreatography in Small Children and Adolescents. Surgical laparoscopy & endoscopy. 1995; 5(4):296–300. [PubMed: 7551282]
25. Dua K, Miranda A, Santharam R, Ramanujam S, Werlin S. ERCP in the evaluation of abdominal pain in children. Gastrointest Endosc. 2008; 68(6):1081–5. [PubMed: 18640674]
26. Halvorson L, Halsey K, Darwin P, Goldberg E. The safety and efficacy of therapeutic ERCP in the pediatric population performed by adult gastroenterologists. Dig Dis Sci. 2013; 58(12):3611–9. [PubMed: 24026405]

27. Limketkai BN, Chandrasekhara V, Kalloo AN, Okolo PI 3rd. Comparison of performance and safety of endoscopic retrograde cholangiopancreatography across pediatric age groups. Dig Dis Sci. 2013; 58(9):2653–60. [PubMed: 23709156]
28. Otto AK, Neal MD, Slivka AN, Kane TD. An appraisal of endoscopic retrograde cholangiopancreatography (ERCP) for pancreaticobiliary disease in children: our institutional experience in 231 cases. Surgical endoscopy. 2011; 25(8):2536–40. [PubMed: 21359895]
29. Pfau PR, Chelimsky GG, Kinnard MF, Sivak MV, Wong RCK, Isenberg GA, et al. Endoscopic retrograde cholangiopancreatography in children and adolescents. Journal of Pediatric Gastroenterology and Nutrition. 2002; 35(5):619–23. [PubMed: 12454575]
30. Rescorla FJ, Plumley DA, Sherman S, Scherer LR 3rd, West KW, Grosfeld JL. The efficacy of early ERCP in pediatric pancreatic trauma. J Pediatr Surg. 1995; 30(2):336–40. [PubMed: 7738761]
31. Troendle DM, Barth BA. ERCP can be safely and effectively performed by a pediatric gastroenterologist for choledocholithiasis in a pediatric facility. J Pediatr Gastroenterol Nutr. 2013; 57(5):655–8. [PubMed: 24048163]
32. Issa H, Al-Haddad A, Al-Salem AH. Diagnostic and therapeutic ERCP in the pediatric age group. Pediatr Surg Int. 2007; 23(2):111–6. [PubMed: 17149628]
33. Keil R, Snajdauf J, Stuj J, Kalousova J, Nevolova P, Janik V, et al. Endoscopic retrograde cholangiopancreatography in infants and children. Indian journal of gastroenterology : official journal of the Indian Society of Gastroenterology. 2000; 19(4):175–7. [PubMed: 11059184]
34. Saito T, Terui K, Mitsunaga T, Nakata M, Kuriyama Y, Higashimoto Y, et al. Role of Pediatric Endoscopic Retrograde Cholangiopancreatography in an Era Stressing Less-Invasive Imaging Modalities. Journal of Pediatric Gastroenterology and Nutrition. 2014; 59(2):204–9. [PubMed: 24762457]
35. Shteyer E, Wengrower D, Benuri-Silbiger I, Gozal D, Wilschanski M, Goldin E. Endoscopic retrograde cholangiopancreatography in neonatal cholestasis. J Pediatr Gastroenterol Nutr. 2012; 55(2):142–5. [PubMed: 22790901]
36. Taj MA, Leghari A, Qureshi S, Ghazanfar S, Niaz SK, Quraishy MS. Endoscopic retrograde cholangiopancreatography: a therapeutic modality in children and adolescents. JPMA The Journal of the Pakistan Medical Association. 2012; 62(2):98–101. [PubMed: 22755366]
37. Teng R, Yokohata K, Utsunomiya N, Takahata S, Nabae T, Tanaka M. Endoscopic retrograde cholangiopancreatography in infants and children. Journal of gastroenterology. 2000; 35(1):39–42. [PubMed: 10632539]
38. Vegting IL, Tabbers MM, Taminiau J, Aronson DC, Benninga MA, Rauws EAJ. Is Endoscopic Retrograde Cholangiopancreatography Valuable and Safe in Children of All Ages? Journal of Pediatric Gastroenterology and Nutrition. 2009; 48(1):66–71. [PubMed: 19172126]
39. Cotton PB, Eisen GM, Aabakken L, Baron TH, Hutter MM, Jacobson BC, et al. A lexicon for endoscopic adverse events: report of an ASGE workshop. Gastrointest Endosc. 2010; 71(3):446–54. [PubMed: 20189503]
40. Thakkar K, El-Serag HB, Mattek N, Gilger MA. Complications of pediatric EGD: a 4-year experience in PEDS-CORI. Gastrointest Endosc. 2007; 65(2):213–21. [PubMed: 17258979]
41. Thakkar K, El-Serag HB, Mattek N, Gilger M. Complications of pediatric colonoscopy: a five-year multicenter experience. Clin Gastroenterol Hepatol. 2008; 6(5):515–20. [PubMed: 18356115]
42. Kapral C, Duller C, Wewalka F, Kerstan E, Vogel W, Schreiber F. Case volume and outcome of endoscopic retrograde cholangiopancreatography: Results of a nationwide Austrian benchmarking project. Endoscopy. 2008; 40(8):625–30. [PubMed: 18680074]
43. Adler DG, Lieb JG 2nd, Cohen J, Pike IM, Park WG, Rizk MK, et al. Quality indicators for ERCP. Gastrointest Endosc. 2015; 81(1):54–66. [PubMed: 25480099]
44. Jorgensen J, Kubiliun N, Law JK, Al-Haddad MA, Bingener-Casey J, Christie JA, et al. Endoscopic retrograde cholangiopancreatography (ERCP): core curriculum. Gastrointest Endosc. 2016; 83(2):279–89. [PubMed: 26708081]
45. Troendle DM, Abraham O, Huang R, Barth BA. Factors associated with post-ERCP pancreatitis and the effect of pancreatic duct stenting in a pediatric population. Gastrointestinal Endoscopy. 2015; 81(6):1408–16. [PubMed: 25686874]

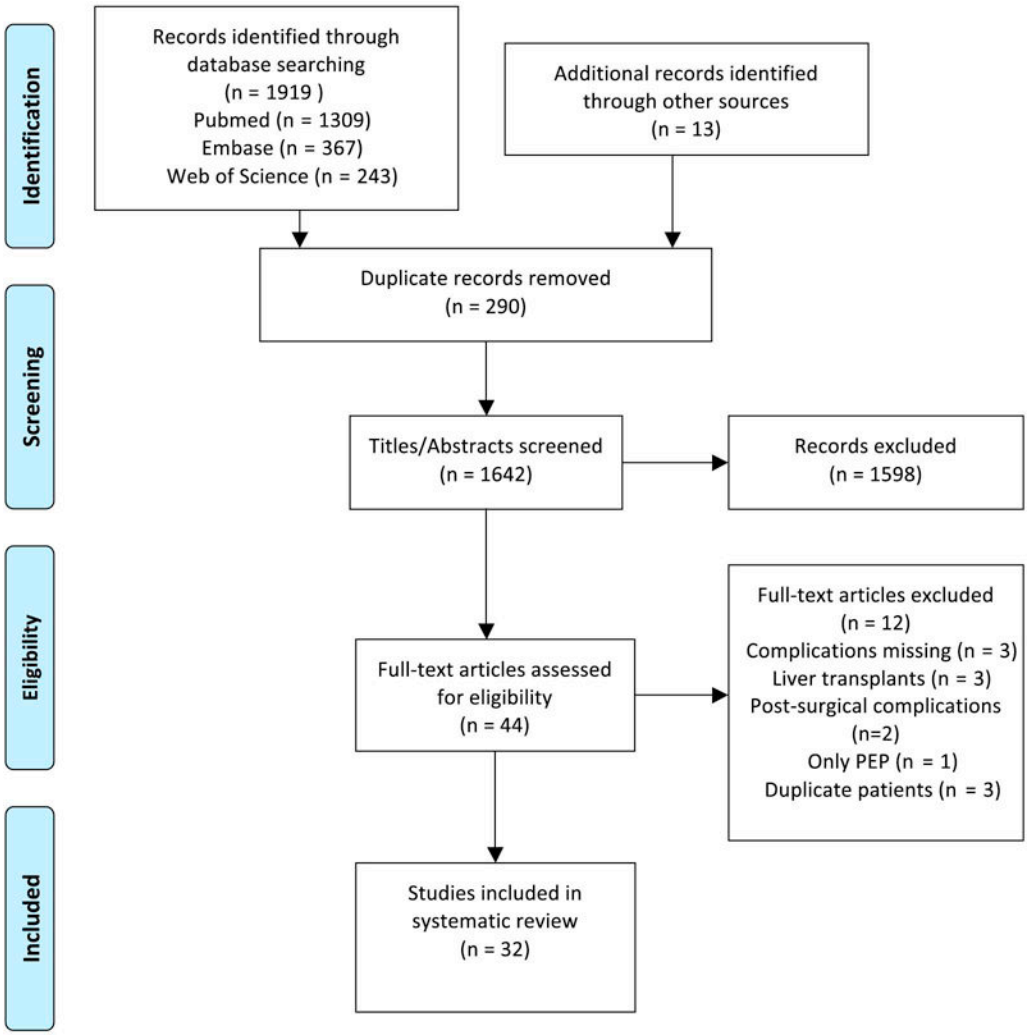

Figure 1.
PRISMA flowchart of literature search

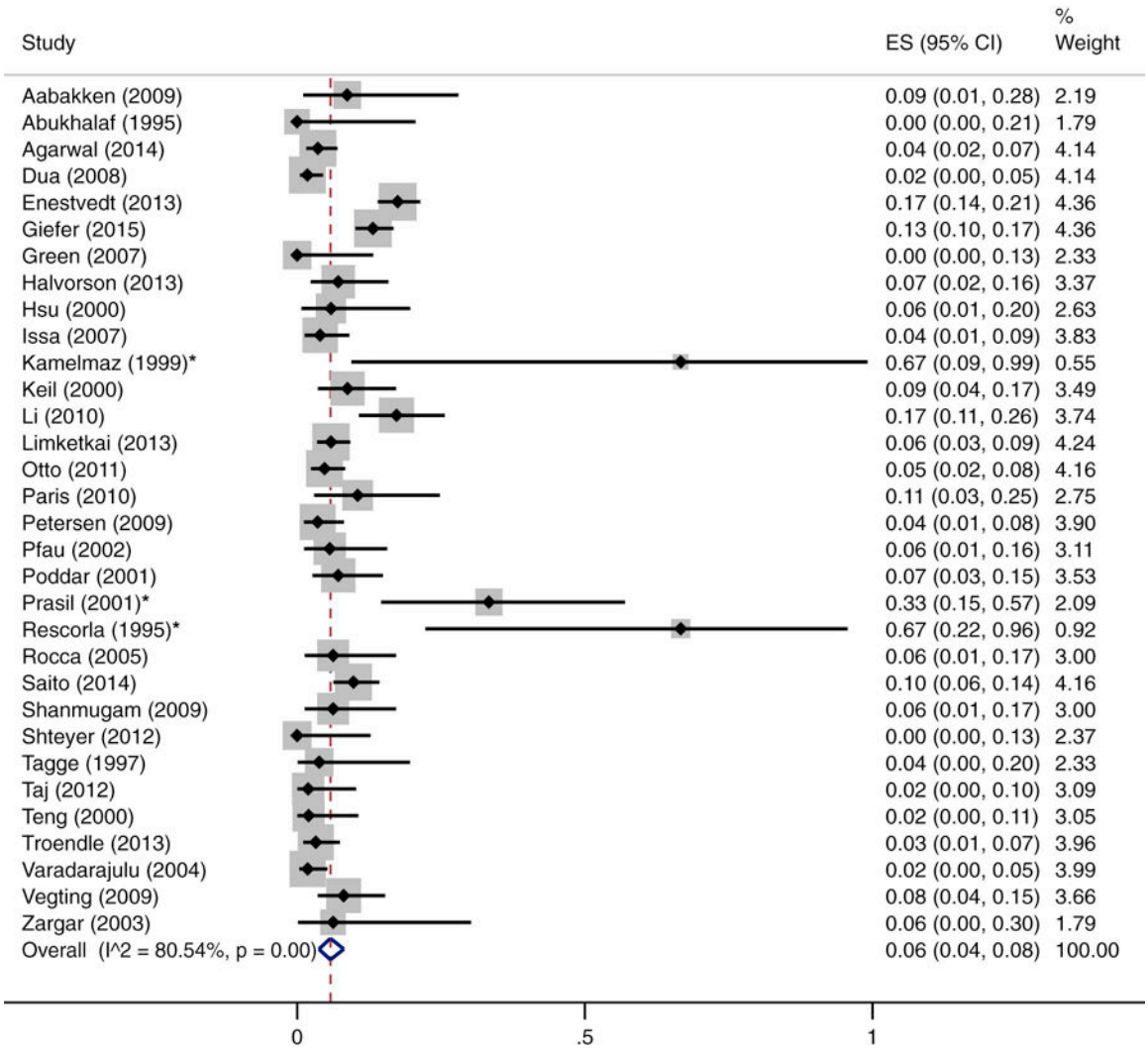

Figure 2.
Pooled estimate of ERCP complications in pediatric patients. Studies removed as outliers.

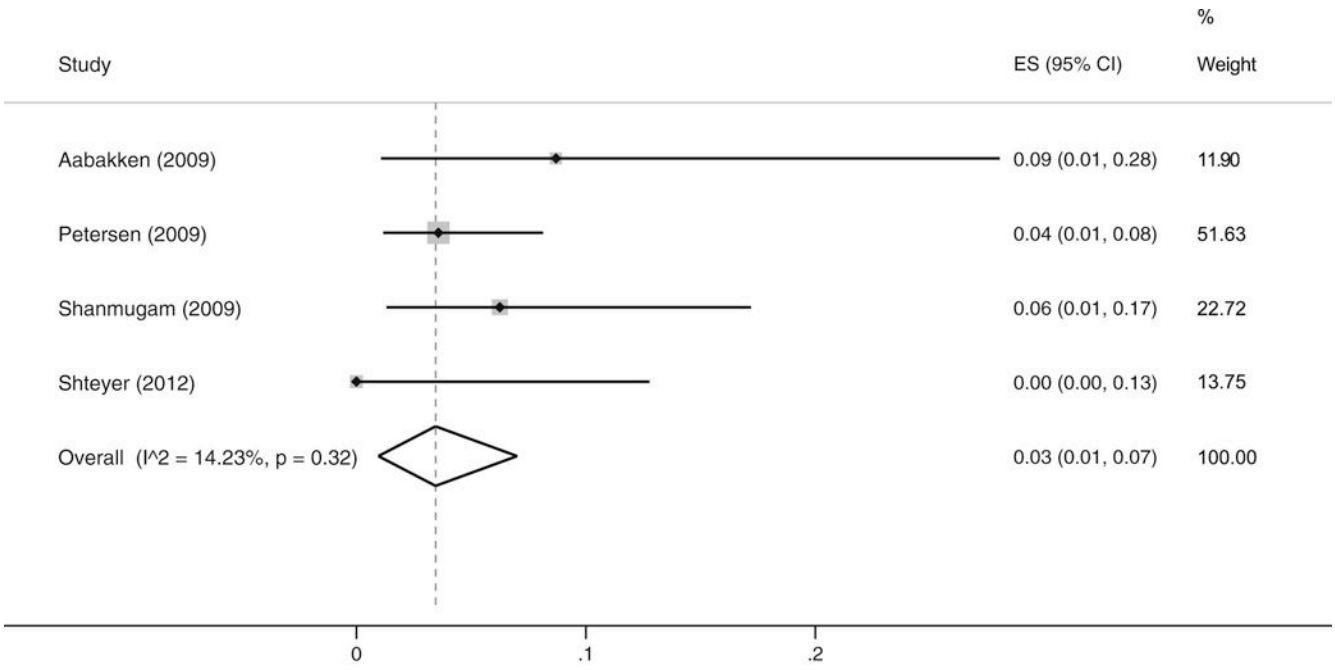

Figure 3.

(online only) Pooled Estimate of Proportion of Complications in ERCPs Performed Only in Neonatal Cholestasis. Pooled estimate takes into account the variability in study size as well as the heterogeneity of each of theses studies assigning a weight and then combines the proportions according to this weight.

Table 1

Diagnostic ERCP in Neonatal Cholestasis Study Characteristics

Author, year	Patients (n)	Procedures (n)	Male (%)	Age Means (years)	Age Range (years)	Endoscopist Training	Complications (n)
Aabakken, 2009	22	23	NR *	0.2	0.06–0.7	Adult	2
Petersen, 2009	140	140	NR *	0.16	0.04–0.48	Other/Unknown	5
Shanmugam, 2009	48	48	50	0.16	0.05–0.27	Adult	3
Shteyer, 2012	27	27	52	0.15	0.09–0.24	Adult	0

* NR= Not Reported

Table 2

ERCP and Study Characteristics in Studies Including All Age Ranges

Author, year	Procedures (n)	Patients (n)	Age Mean (years)	Age Range (years)	Endoscopist Training‡	Diagnosis§ (n)			Interventional (%)	Complications (%)
						B	P	O		
Kamelmaz, 1999	3	3	12.8	6.5–16	O/U	0	3	0	33%	67%
Rescorla, 1995	6	6	4.8	2–8	O/U	0	6	0	0%	67%
Abukhalaf, 1995	16	16	10.5	0.17–18	O/U	9	4	0	25%	0%
Zargar, 2003	16	16	12.6	7–16	Adult	7	0	9	100%	6%
Prasil, 2001	21	20	11.3	4–17	Adult	15	5	0	48%	33%
Green, 2007	26	19	13	7–16	O/U	11	14	1	88%	0%
Tagge, 1997	26	26	10.1	0.5–19	O/U	21	5	0	50%	4%
Hsu, 2000	34	22	10.7	1.5–17	O/U	6	18	0	68%	6%
Paris, 2010	38	29	10.3	3–17	Adult	9	29	0	34%	11%
Rocca, 2005	48	38	10	0.08–17	Adult	24	14	0	77%	6%
Teng, 2000	50	42	NR*	0.16–15	O/U	31	11	0	12%	2%
Taj, 2012	52	40	13.6	3–18	Adult	19	19	2	92%	2%
Pfau, 2002	53	43	13.5	1–18	Adult	20	14	17	45%	6%
Halvorson, 2013	70	45	12	6–17	Adult	32	22	0	93%	7%
Keil, 2000	80	59	11.2	0.05–18	O/U	41	16	2	58%	9%
Poddar, 2001	84	72	8.8	0.92–14	Pediatric	52	17	8	26%	7%
Vegting, 2009	99	61	7	0.008–16.9	Adult	51	10	0	61%	8%
Li, 2010	110	42	16	NR*	Adult	0	42	0	100%	17%
Issa, 2007	125	125	13.3	5–18	O/U	115	9	0	50%	4%
Troendle, 2013	154	65	15.2	0.08–18.4	Pediatric	50	15	0	42%	3%
Varadarajulu, 2004	163	116	9.3	0.08–17	Adult	60	49	7	47%	2%
Agarwal, 2014	221	172	13.8	5–18	Adult	0	172	0	71%	4%
Dua, 2008	224	185	NR*	0–18	Adult	71	43	71	33%	2%
Otto, 2011	231	167	11.4	0.17–21	Adult	31	148	0	69%	5%
Saito, 2014	235	220	4	0.02–20	O/U	181	5	32	3%	10%
Limketkai, 2013	289	154	11.5	1–17	O/U	132	220	8	85%	6%
Giefer, 2015	425	276	13.6	0.2–18	Both	194	210	11	81%	13%

Author, year	Procedures (n)	Patients (n)	Age Mean (years)	Age Range (years)	Endoscopist Training‡	Diagnosis§ (n)			Interventional (%)	Complications (%)
						B	P	O		
Enestvedt, 2013	429	296	14.9	0.25–21	Adult	268	51	92	64%	17%

*NR= Not Reported

‡O/U= Other/Unknown

§B=Biliary, P=Pancreatic, O=Other

J Pediatr. Author manuscript; available in PMC 2017 December 01.

Table 3

Study Characteristics of 32 Included Studies

Author, year	Center	Study Period	Patients (n)	Procedures (n)	Mean Age (years)	Age Range (years)
Aabakken, 2009 (14)	University of Oslo	1999 – 2006	22	23	0.2	0.06 – 0.7
Abukhalaf, 1995 (27)	Jordan University Hospital	1990 – 1993	16	16	10.5	0.17 – 18
Agarwal, 2014 (15)	University of Hyderbad	2010 – 2011	172	221	13.8	5 – 18
Dua, 2008 (28)	Children's Hospital of Wisconsin	1994 – 2004	185	224	0	0 – 18
Enestvedt, 2013 (7)	Children's Hospital of Philadelphia	1993 – 2011	296	429	14.9	0.25 – 21
Giefer, 2015 (16)	Seattle Children's Hospital	1994 – 2011	276	425	13.6	0.2 – 18
Green, 2007 (6)	De Vos Children's Hospital, MI	2000 – 2005	19	26	13	7 – 16
Halvorson, 2013 (29)	University of Maryland	2003 – 2011	45	70	12	6 – 17
Hsu, 2000 (17)	UC Davis and U of South Carolina	1994 – 1996	22	34	10.7	1.5 – 17
Issa, 2007 (36)	Qatif Central Hospital	1993 – 2005	125	125	13.3	5 – 18
Kamelmaz, 1999 (5)	Marshall University, WV	NR *	3	3	12.8	6.5 – 16
Keil, 2000 (37)	University of Prague	1995 – 1999	59	80	11.2	0.05 – 18
Li, 2010 (20)	Changhai Hospital, China	1997 – 2009	42	110	16	NR *
Limketkai, 2013 (30)	Johns Hopkins University	1998 – 2011	154	289	11.5	1 – 17
Otto, 2011 (31)	University of Pittsburg	1992 – 2008	167	231	11.4	0.17 – 21
Paris, 2010 (21)	St Justine University, Canada	1990 – 2007	29	38	10.3	3 – 17
Petersen, 2009 (22)	Hanover Medical School, Germany	2001 – 2008	140	140	0.16	0.04 – 0.48
Pfau, 2002 (32)	Rainbow Babies, OH	NR *	43	53	13.5	1 – 18
Poddar, 2001 (8)	Chandigarh, India	1995 – 2000	72	84	8.8	0.92 – 14
Prasil, 2001 (23)	McGill University, Montreal children's	1990 – 1999	20	21	11.3	4 – 17
Rescorla, 1995 (33)	Riley Children's Hospital, IN	1988 – 1993	6	6	4.8	2 – 8
Rocca, 2005 (24)	Turin, IT	1996 – 2002	38	48	10	0.08 – 17
Saito, 2014 (37)	Chiba University, Japan	1980 – 2011	220	235	4	0.02 – 20
Shanmugam, 2009 (25)	London, Kings College Hospital	1997 – 2007	48	48	0.16	0.05 – 0.27
Shteyer, 2012 (38)	Hadassah-Hebrew University, Israel	2000 – 2010	27	27	0.15	0.09 – 0.24
Tagge, 1997 (18)	South Carolina	1990 – 1995	26	26	10.1	0.5 – 19
Taj, 2012 (39)	Civil Hospital Karachi	2007 – 2010	40	52	13.6	3 – 18
Teng, 2000 (40)	Kyushu University	NR *	42	50	0	0.16 – 15

Author, year	Center	Study Period	Patients (n)	Procedures (n)	Mean Age (years)	Age Range (years)
Troendle, 2013 (34)	University of Texas Southwestern	2006 – 2012	65	154	15.2	0.08 – 18.4
Varadarajulu, 2004 (19)	Birmingham and Charleston	1994 – 2002	116	163	9.3	0.08 – 17
Vegting, 2009 (41)	Emma Children's Hospital, Netherlands	1995 – 2005	61	99	7	0.008 – 16.9
Zargar, 2003 (26)	Kashmir, India	1998 – 2001	16	16	12.6	7 – 16

*NR= Not Reported