



# Duodenal atresia and associated intestinal atresia: a cohort study and review of the literature

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## Abstract

**Purpose** To determine the true incidence of associated intestinal atresia (AIA) in infants with duodenal atresia (DA) and to analyze whether the surgical approach, open versus laparoscopic, would impact on patient outcome when AIA is present.

**Methods** *Cohort study* We review all DA infants treated at our institution (2001–2016) and analyzed the outcome of those with AIA. *Systematic review/meta-analysis* Using a defined search strategy and according to PRISMA guidelines, two investigators independently identified all studies on DA and searched cases of AIA to determine its incidence. Data are mean ± SD.

**Results** *Cohort study* Of 140 DA infants, 10 (7%) had AIA (4 type I, 4 type III, 2 type II). All type I AIA (webs) were found in the duodenum. *Systematic review/meta-analysis* Of 840 studies, 18 were included (2026 infants). The incidence of AIA was  $2.8 \pm 1.6\%$ . The incidence of missed AIA was  $0.8 \pm 2.4\%$ . Three comparative studies (759 infants) showed higher risk of missed AIA following laparoscopic ( $2.9 \pm 2.4\%$ ) than open repair ( $0.3 \pm 0.1\%$ ;  $p < 0.01$ ).

**Conclusions** The incidence of AIA in DA infants is low and the risk of missing it is higher at laparoscopy than at laparotomy. Regardless the approach, surgeons should carefully investigate bowel continuity to avoid the risk of missing AIA.

**Keywords** Jejunal atresia · Ileal atresia · Cohort study · Systematic review · Meta-analysis

## Introduction

Duodenal atresia (DA) is a cause of congenital intestinal obstruction that occurs in 1 in 5000–10,000 live births and affects more commonly boys than girls [1, 2]. There are various theories on DA pathophysiology, among which the most accredited explains the atresia as a defect of recanalization of the primitive duodenum between the 8th and the 10th week of gestation [3, 4]. This is different from the principal cause of atresia and stenosis in other parts of the small

bowel, which are considered to result from vascular accidents [5]. It is well known that about a third of babies with DA has trisomy 21 [1, 2, 5–8]. Moreover, more than 50% of infants with DA have an associated congenital anomaly, either alone or as part of an association, such as VACTERL [3, 4]. These associated anomalies can be in other organs or systems, such as the heart and the genitourinary system, but most commonly they are found in the gastrointestinal tract [1, 3, 4, 8, 9]. In the latter case, the most commonly associated anomalies are annular pancreas, intestinal malrotation, and intestinal atresia and/or stenosis [1, 4].

Infants with DA are treated with surgery, which is performed to re-establish intestinal continuity to enable feeding. The classical surgical repair of DA is carried out with a duodeno-duodenostomy, but over the years several variations have been described; these include modifications in the anastomosis creation, such as the diamond shaped technique described by Kimura et al. [10], in the type of anastomosis, with the alternative duodeno-jejunostomy [11], and in the surgical approach, that in the last two decades has included the laparoscopic repair [2, 5, 12–16]. Regardless the technique employed, the surgeon is expected to carefully inspect the entire bowel before completing the duodenal repair, so

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to rule out potential associated atretic or stenotic intestinal segments [16–18]. The surgeon should explore the duodenal segment proximal to the atresia to exclude a possible web, as well as the distal small and large bowel [18]. To confirm intestinal continuity, the surgeon would typically flush the proximal and distal bowel with warm normal saline, as with external bowel inspection alone an incomplete intestinal web or windsock might be overlooked [18]. With the advent of laparoscopic DA repair, the assessment of the bowel for possible atretic segments was called into question. In his earliest report on DA laparoscopic repair, Rothenberg was the first to report that laparoscopy had the possible disadvantage of making the evaluation of the distal bowel difficult to perform [19]. Since then, a number of studies have proved that DA laparoscopic repair is feasible and effective [12–16]. Nevertheless, the exact incidence of associated intestinal atresia in infants with DA remains unknown, with series reporting discordant figures.

Herein, we reviewed our center experience and combined it with a systematic review of the literature to determine the true incidence of associated intestinal atresia in infants with DA. Moreover, we analyzed whether the surgical approach, open versus laparoscopic, would have an impact on patient outcome when an associated intestinal atresia is present.

## Materials and methods

### Cohort study

Following ethical approval (REB #1000055682), we reviewed the medical charts of all patients who were operated on for duodenal atresia at our Institution between 2001 and 2016. In our analysis, we included all infants with duodenal atresia associated with another atresia. Data collected included gender, gestational age, birth weight, prenatal diagnosis, associated anomalies, duration of hospitalization, age at surgery, operative technique, intraoperative findings, weight at discharge, and follow-up. The type of duodenal atresia was classified according to the Gray and Skandalakis classification [20], whereas that of associated intestinal atresia according to the Bland-Sutton classification [21].

### Systematic review and meta-analysis

Both the systematic review and the meta-analysis were drafted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [22]. Two different health librarians were involved at the Gerstein Science Information Centre (University of Toronto, ON, Canada) and the Bibl@Ud'A (University of Chieti-Pescara, Italy). The present study was registered on PROSPERO (CRD42018109164), the international prospective

register of systematic reviews [23]. A systematic review of the literature was made using a defined search strategy. Two investigators (MEM and GL) independently searched scientific databases (PubMed, Medline, Cochrane Collaboration, Embase and Web of Science) using a combination of keywords (Table 1). MeSH headings and terms used were “duodenal atresia”, “duodenal atresia AND intestinal atresia”, and “duodenal atresia AND associated intestinal atresia” (Supplementary file 1). Case reports, opinion articles, experimental studies and case series with less than 10 patients were excluded. All grey literature publications (i.e. reports, theses, conference proceedings, bibliographies, commercial documentations, and official documents not published commercially) were excluded. The full text of the potentially eligible studies was retrieved and independently assessed for eligibility by the same two investigators. Any disagreement between them over the eligibility of particular studies was resolved through discussion with a third author (AZ).

For the meta-analysis, we included only studies comparing open versus laparoscopic DA repair and measured the proportion of missed DA associated intestinal atresia. The meta-analysis was conducted with RevMan 5.3 [24], using the random-effects model to produce risk ratio (RR) for categorical variables and mean differences (MD) for continuous variables, along with 95% confidence intervals (CI). We produced  $I^2$  values to assess homogeneity and quantify the dispersion of effect sizes. Data were compared using Fisher's exact test and are expressed as mean  $\pm$  SD. When median and range were reported, mean  $\pm$  SD were estimated, as reported [25].

**Table 1** Inclusion criteria of systematic review

Publication	
Language	Any
Date	After 1950
Subject	Human studies
Study type	Retrospective
	Prospective
	Case-control
	Cohort
Excluded	Case reports
	Case series
	Letters
	Editorials
	Grey literature
	Keywords
	Intestinal atresia
	Associated intestinal atresia
	Open repair duodenal atresia
	Laparoscopic repair duodenal atresia

**Quality assessment**

Risk of bias for individual studies was assessed in duplicate (MEM and GL) using the methodological index for nonrandomized studies (MINORS) [26]. Differences between the two reviewers (MEM and GL) were resolved through consensus and discussion with another author (AZ). The total score for this 12-item instrument ranges 0–24 points with a validated “gold standard” cut-off of 19.8. Two authors (PLC and AZ) independently evaluated the present systematic reviews and meta-analysis using A Measurement Toll to Assess Systematic Reviews (AMSTAR) [27]. The PRISMA checklist of our study was then completed [22].

**Table 2** Associated anomalies in the present cohort study

Associated anomalies	All DA (n = 140)	DA + AIA (n = 10)
Gastrointestinal (GERD, malrotation)	12	2
Cardiovascular (VSD, PFO, HLHS, tetralogy of fallot, coarctation of aorta)	26	1
Down syndrome	27	–
VACTERL	10	2
Genitourinary (renal agenesis or hypoplasia)	5	1
Respiratory	2	–
Others (neurological, orthopedic)	17	1

DA duodenal atresia, AIA associated intestinal atresia, GERD gastroesophageal reflux disease, VSD ventricular septal defect, PFO patent foramen ovale, HLHS hypoplastic left heart syndrome, VACTERL vertebral anomalies, anorectal, malformations, cardiovascular anomalies, tracheoesophageal fistula, esophageal atresia, renal and/or radial anomalies, and limb defects

**Table 3** Cohort study: patient with duodenal atresia and associated intestinal atresia

Pt. #	Gender	Gestational age (weeks)	Birth weight (g)	Type of DA	Type of associated intestinal atresia
1	M	37	2430	3	IV—(jejunoileal)
2	M	38	1610	3	IIIa—(jejunal)
3	M	34	2155	2	IIIb—(jejunoileal)
4	F	33	2500	1	I—(duodenal)
5	F	33	2230	3	IIIb—(jejunoileal)
6	M	36	3060	3	I—(duodenal)
7	M	36	2910	2	IIIb—(jejunoileal)
8	F	38	4260	2	I—(duodenal)
9	M	36	2670	1	I—(duodenal)
10	M	31	1772	3	IV—(jejunoileal + colonic)

DA duodenal atresia, AIA associated intestinal atresia

**Results**

**Cohort study**

During the study period, we identified 140 babies with a diagnosis of DA (75 males, 65 females), who underwent surgical repair at our institution. The mean gestational age was  $36 \pm 3$  days and mean birth weight was  $2549 \pm 701$  g. Eighty seven of 140 children had a prenatal diagnosis of DA. Twenty-seven babies (19%) had trisomy 21, while 10 patients (7%) had a diagnosis of VACTERL association (Table 2). Fifteen newborns (11%) had an associated esophageal atresia. Mean age at surgery was  $4.3 \pm 4$  days (range 1–37 days). Twelve (9%) infants died before being discharged due to the severity of associated anomalies. Mean length of hospitalization was  $45 \pm 53$  days (range 9–335 days) and mean weight at discharge was  $3194 \pm 945$  g.

All 140 neonates with DA underwent open repair, of whom 85 had a duodeno-duodenostomy and 55 a duodeno-jejunosomy. All 140 neonates were intraoperatively investigated for an associated intestinal atresia and 10 (7%) were found to have it (Table 3). Among these 10 infants, 7 were males. Mean birth weight was  $2560 \pm 752$  g and mean GA  $35 \pm 2$  days. Seven babies had a prenatal diagnosis of DA. None of the 10 neonates had a Trisomy 21 or other genetic anomalies (Table 2). Mean age at surgery was  $4.4 \pm 4$  days, ranging from 1 to 7 days. Four infants had a type I associated atresia within the duodenum, 3 had a type IIIb apple peel, 2 had multiple type IV intestinal atresia, and 1 had a type IIIa jejunal atresia. Moreover, half of the associated intestinal atresia (5/10 patients) was detected in patients with type 3 DA (Table 3). One patient underwent a re-laparotomy for a missed duodenal web, proximal to the first DA. Mean length of hospital stay was  $63 \pm 73$  days (range 18–221 days) and mean weight at discharge was  $3906 \pm 1263$  g. Three fatalities occurred in this group of patients, as a result of aspiration

pneumonia (patient #6), and complications of intestinal failure (patient #1 and #2).

### Systematic review

Of 840 titles and abstracts screened, 61 full-text articles were analyzed and 18 papers and the present cohort study met the inclusion criteria (2026 infants, Fig. 1) [1, 4, 5, 7–10, 16, 28–37]. The incidence of an associated intestinal atresia was  $2.8 \pm 1.6\%$  (57/2026 infants, range 0.5–7.1%, Table 4). The reported incidence of missed associated intestinal atresia during DA repair (both open and laparoscopic) was  $0.8 \pm 2.4\%$  (9/1168 infants, range 0–9.5%) (Table 4).

### Meta-analysis

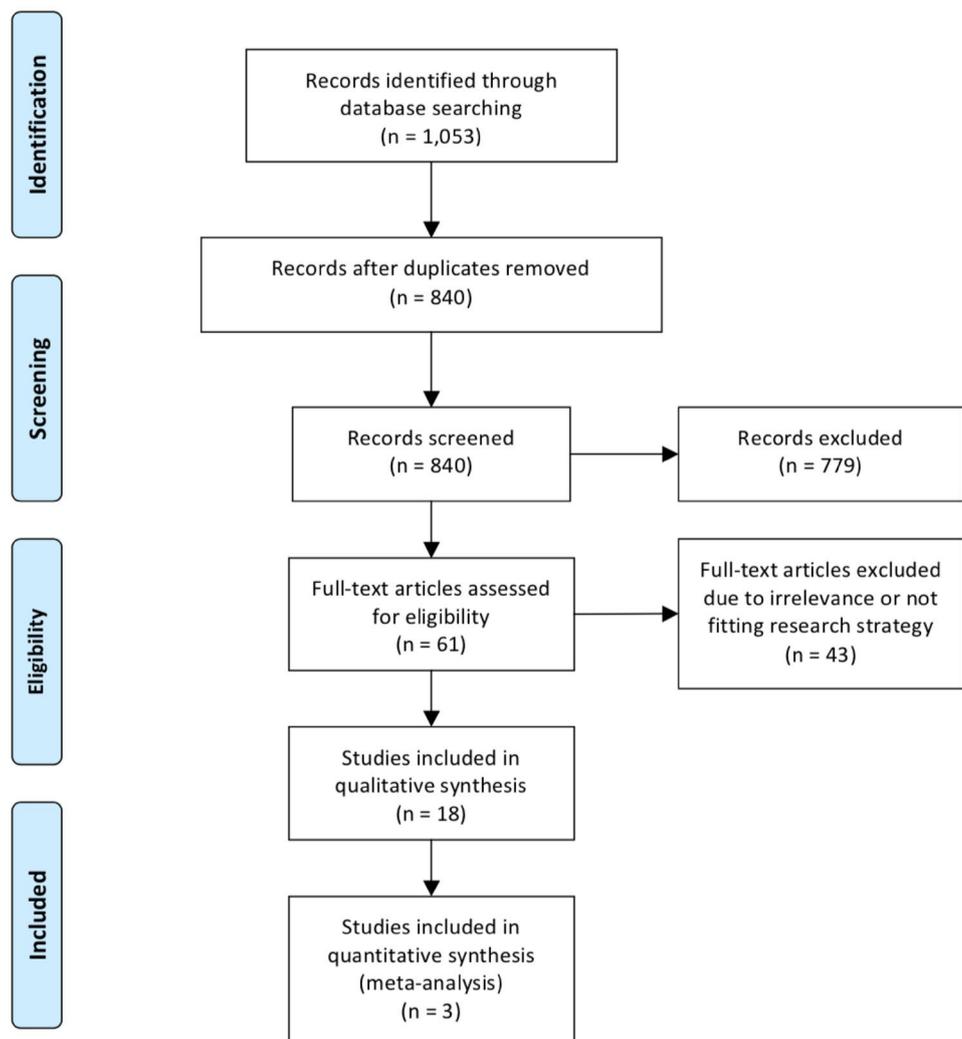
Three comparative retrospective studies were included (759 infants) [16, 34, 35]. We found that laparoscopic DA repair was associated with a higher risk of missed associated

atretic segments ( $3 \pm 2\%$ , 3/101 infants) than open DA repair ( $0.3 \pm 0.1\%$ , 2/658 infants;  $p < 0.01$ ; RR 9.0, 95% CI 1.8–45.7;  $I^2 = 0\%$ ; Fig. 2).

### Discussion

The present study shows that DA is associated with another intestinal atresia in around 3% of patients. This incidence was extrapolated from all available case series reported in the literature and from our own single-center experience, with more than 2000 infants with DA involved, thus making it the largest series ever published on the topic. The low incidence of this association could be ascribed to the different embryological etiologies between DA and small bowel atresia [16]. Other studies have investigated the incidence of DA associated intestinal atresia and reported different frequencies. In 1998, Dalla Vecchia et al. reported their single-center experience and calculated an incidence

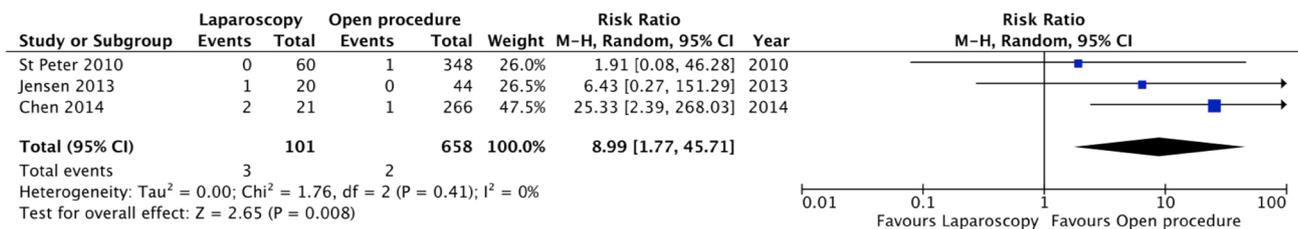
**Fig. 1** Diagram of workflow in the systematic review and meta-analysis



**Table 4** Studies included in the systematic review (with the present cohort study)

Author	Year publication	n Duodenal atresia	Associated intestinal anomalies	%	Missed AIA (%)
Weber et al. [28]	1986	41	1	2.4	Open 1/41 (2.4)
Kimura et al. [10]	1990	44	2	4.5	
Spigland et al. [29]	1990	33	2	6	
Dalla Vecchia et al. [30]	1998	138	9	6.5	
Murshed et al. [9]	1999	275	7	2.5	
Lawrence et al. [31]	2000	29	1	3.4	
Rao et al. [32]	2001	15	1	6.6	
Escobar et al. [1]	2004	169	4	0.6	Open 1/169 (0.6)
Mustafawi et al. [7]	2008	77	2	2.6	
Choudhry et al. [4]	2009	61	4	6.6	
Burjonrappa et al. [5]	2011	59	1	1.7	Open 1/59 (1.7)
St Peter et al. [16]	2010	408	2	0.5	Lap 0/60 (0) Open 1/348 (0.3)
Sarin et al. [33]	2012	18	1	5.5	
Jensen et al. [34]	2013	64	1	1.6	Lap 1/20 (5) Open 0/44 (0)
Chen et al. [35]	2014	287	3	1	Lap 2/21 (9.5) Open 1/266 (0.4)
Kumar et al. [36]	2016	31	1	3.2	
Rattan et al. [8]	2016	81	4	4.9	
Cho et al. [37]	2017	56	1	1.8	
Present cohort study	2018	140	10	7.1	Open 1/140 (0.7)
<b>Total</b>		<b>2026</b>	<b>57</b>	<b>2.8</b>	

AIA associated intestinal atresia, *Lap* laparoscopic procedure, *Open* laparotomic approach



**Fig. 2** Forest plot comparison of the incidence of missed associated intestinal atresia comparing laparoscopy versus open procedure

of DA associated intestinal atresia of 6.5% over a cohort of 138 infants with DA [30]. This is similar to the incidence reported in our cohort. Conversely, in a multicenter retrospective study comprising 408 infants with DA, St. Peter et al. reported an incidence of jejunoileal atresia observed during DA repair of 0.5% [16]. It is difficult to speculate on the discrepancy of the reported incidence rates across the studies. Nonetheless, the proportion of infants with DA and an associated intestinal atresia remains low.

The interest in this specific aspect of DA surgery arose with the advent of laparoscopy. Since then, many surgeons opted for the minimally invasive approach, demonstrating its safety and feasibility [2, 12–15, 38]. Among the reported advantages of laparoscopic DA repair were the better

cosmetic results and the less manipulation of the bowel with potential lower risk of postoperative adhesive bowel obstruction [6, 34, 37–39]. However, since the beginning of the laparoscopic experience, surgeons realized that the inspection of the proximal and distal bowel to rule out an associated intestinal atresia was difficult [19]. It is known, in fact, that if missed, an associated atresia or web could cause postoperative bowel obstruction, longer hospital admission, longer time on parenteral nutrition due to delay in establishing feeds, more imaging studies to achieve the diagnosis, and indeed the need for further neonatal surgical intervention. On this point, the literature remains divided between those who recommend the laparoscopic approach and those who opt for an open repair [1, 6, 12, 13, 16, 34, 35, 37–39].

**Table 5** Risk of bias assessment for individual studies using methodological index for nonrandomized studies (MINORS) [24]

Item	St Peter et al. [16]	Jensen et al. [34]	Chen et al. [35]
1. A clearly stated aim	2	2	2
2. Inclusion of consecutive patients	2	2	2
3. Prospective collection of data	0	0	0
4. Endpoints appropriate to the aim of the study	2	2	2
5. Unbiased assessment of the study endpoint	0	0	0
6. Follow-up period appropriate to the aim of the study	0	0	2
7. Loss to follow-up less than 5%	0	0	2
8. Prospective calculation of the study size	0	0	0
9. An adequate control group	2	2	2
10. Contemporary groups	2	2	2
11. Baseline equivalence of groups	0	2	2
12. Adequate statistical analyses	1	2	2
Total score	11	14	18

0 = not reported, 1 = reported but inadequate, 2 = reported and adequate

Indeed, the latter approach allows the manual inspection of the intestine and facilitates the possibility to detect an associated intestinal atresia.

In our study, we analyzed the papers that compared open versus laparoscopic DA repair, specifically looking for the incidence of missed associated intestinal atresia, and we found that the risk is significantly higher during laparoscopy than during open DA repair. In our case series, we also analyzed the type of DA associated intestinal atresia, which we classified according to the Bland-Sutton classification. Interestingly, we found that the most commonly associated intestinal atresia was type I (windsock or web), which in all our cases was located in the duodenum. In fact, in our series, all cases of associated jejunoileal atresia were type III or IV: these are the types of atresia that present with a mesenteric defect and potentially could be more easily diagnosed on external inspection, possibly without the need for testing the patency of the bowel lumen. In this respect, our study shows that surgeons should definitely examine the duodenum, as this is the location where most likely another atresia could be found, but also that an external bowel inspection, which is feasible with the laparoscopic approach, could be sufficient in the majority of cases.

We acknowledge that our present study has some limitations, which are mainly due to the fact that systematic reviews and meta-analyses rely on the quality of studies and data available in the literature. In our meta-analysis, all three studies included were retrospective. None of the studies reached the gold standard cut-off on MINORS of 19.8 out of 24 (Table 5). None of the papers provided sample size calculations, and none of the studies reported a blinded evaluation of objective endpoints. Furthermore, length of follow-up was not mentioned in two studies [16,

34] and statistical analysis was inadequate in one paper [16]. However, when independently assessed by two authors using AMSTAR, the present systematic reviews and meta-analysis received a relevant score (Supplementary file 2). The PRISMA checklist of our study was then completed (Supplementary file 3).

In conclusion, our study shows that the true incidence of DA associated intestinal atresia is low. Moreover, the cases presenting with an associated web or windsock, i.e. those types of atresia that could be more easily missed, are rarely found in the jejunum or in the ileum, rather in the duodenum. Nevertheless, the risk of missing a second intestinal atresia when performing DA repair remains a potential complication that surgeons should consider when counseling parents. Our review shows that this risk is higher when the DA repair is achieved laparoscopically than with an open approach. For this reason, regardless the surgical approach chosen for the DA repair, surgeons should carefully investigate the bowel continuity to avoid the risk of missing an associated intestinal atresia.

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### Compliance with ethical standards

**Conflict of interest** Authors have no potential conflicts of interest for this study.

**Ethical approval** Ethical approval REB #1000055682. Not applicable in the Systematic Review and Meta-Analysis.

**Informed consent** Not applicable, since the study was a review of the medical charts of patients, plus a Systematic Review and Meta-Analysis.

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