

# The prevalence of digestive tract defects in East China: A population-based study

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## Abstract

The prevalence of congenital digestive tract defects among Chinese people is rarely reported. The aim of this study was to investigate the incidence of digestive tract defects in mainland China and reported the clinical outcomes of these cases. This study describes a local population-based study of registered births in Jiaying, China from January 2015 to December 2019. Prevalence estimates (per 10,000 births) of digestive tract malformations were calculated. We used the  $\chi^2$  test to compare the differences between categorical variables. In this study a total of 76 cases of digestive tract malformations were included. We calculated the following incidence rates per 10,000 births: 1.65 for esophageal atresia; 1.24 for congenital defects of gastric musculature; 2.33 for hypertrophic pyloric stenosis; 3.72 for duodenal and intestinal atresia; 2.25 for congenital malrotation of intestine; 1.45 for Hirschsprung's disease; 4.75 for anal atresia/stricture; and 1.40 for biliary atresia. There were 31 cases (40.8%) of low birth weight (<2500g), 28 cases (36.8%) were premature births (<37 weeks), and 25 cases (32.9%) had concomitant congenital heart disease. This study estimated the incidence of digestive tract malformations, and the findings may provide a foundation for future epidemiologic studies of these congenital diseases in China. In addition, we found that roughly one third of our subjects with digestive tract defects also had concomitant congenital heart disease, suggesting a link between the two

which may warrant further investigation. Moreover, our data will also be helpful in determining the resources needed for basic and public health research into digestive tract malformation in China.

**Keywords:** digestive tract defects, incidence, China, population-based study

## Introduction

Congenital malformation of the digestive tract is a phenotypically and etiologically diverse condition, comprising a group of common congenital malformations caused by various factors during fetal development [1, 2]. These factors include a range of chromosomal anomalies, genetic predisposition, geographic or ethnic population effects, and other unknown factors [3-6]. There have been many population-based epidemiological studies on digestive tract malformations in Europe and America, which showed that the incidence of digestive tract malformation varies by race and country [7-15]. These studies conducted a number of large-sample, population-based retrospective analyses on the epidemic status of neonatal digestive tract malformation, and reported on the incidence, clinical features, and complications of neonatal digestive tract malformation in different regions and time periods. Estimating the prevalence of birth defects is an important basis for understanding the public health burden of these conditions. This information can comprehensively reflect the average level of major risk factors for neonatal

digestive tract malformation in a region, also provide an important reference for the early detection, treatment, and prognosis of neonatal digestive tract malformation in the future [6, 16, 17].

China is a vast territory with a large and fluid population base, so it is difficult to compile very large sample reports focusing on digestive tract malformations in mainland China. At present, the estimated incidence of digestive tract malformations in mainland China is based on epidemiological studies published abroad, and most mainland Chinese studies have focused on clinical experience and genetics [18-24]. And we plan to objectively and comprehensively ascertain the prevalence of congenital digestive tract malformation in one region and countrywide. Therefore, the purpose of this study was to investigate the prevalence of digestive tract defects in the population of Jiaying of East China, using a large database of residents born between 2015 and 2019, in order to gain a clearer picture of the epidemiology of gastrointestinal defects in mainland China.

## Methods

### Data Presentation

The data used in the study were obtained from the birth defect surveillance network of Jiaying Maternal and Child Health Care Hospital which is the main maternal and child healthcare center in Jiaying, and is responsible for the annual registration of births and birth defects in this region. The total permanent population of Jiaying region is approximately 5 million, and the average annual birth rate is between 30,000 and 35,000 [25]. All registries in this study comprised local registered populations, including all births from mothers residing in Jiaying City from January 2015 to December 2019. Data used in this study also included birth

defect registers, with abnormalities diagnosed prenatally, at birth, or within 7 days of delivery. The total number of births covered by the five-year period in this study was 74,294. Following exclusion of 25,920 records from the migrant population, a total of 48,374 local subjects were analyzed in the study, and 1,656 of these had birth defects. Birth defects eligible for inclusion in the study were classified as “the presence of one or more birth defects during the data collection period”.

### Focus: Digestive Tract Defects

All digestive tract defect cases were coded using the WHO International Classification of Disease (ICD) version 10. The digestive tract defects included in this study were esophageal atresia, congenital defects of gastric musculature, hypertrophic pyloric stenosis, duodenal and intestinal atresia, congenital malrotation of intestine, Hirschsprung’s disease, anal atresia/stricture, and biliary atresia, all registered within seven days of birth. As some digestive tract defects such as hypertrophic pyloric stenosis, Hirschsprung’s disease, and biliary atresia are not always detected in the neonatal period, these cases were collected from medical records. In order to confirm the final diagnosis, all surviving children’s parents were interviewed by telephone.

### Data Analysis

The study included 76 cases with digestive tract defects. The total prevalence of digestive tract defects in each year was calculated as the number of cases per 10,000 total births or per 1,000 defects, and 95% confidence intervals (CIs) were derived from the binomial distribution. If the sample size was less than the number that could be used to calculate the 95% CI, then the figure was expressed per 10,000 births. All statistical analyses were performed using R version 3.6.0.

**Table 1:** The overall birth prevalence in Jiaying China from 2015 to 2019.

		2015 (Total birth =8,409)	2016 (Total birth =11,359)	2017 (Total birth =11,365)	2018 (Total birth =8,693)	2019 (Total birth =8,548)	Total (Total birth =48,374)
		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Total Birth	Male	4,410 (52.44)	5,908 (52.01)	5,902 (51.93)	4,462 (51.33)	4,501 (52.66)	25,183 (52.06)
	Female	3,998 (47.54)	5,449 (47.97)	5,642 (48.06)	4,229 (48.65)	4,044 (47.31)	23,362 (48.29)
	Unknown	1 (0.01)	2 (0.02)	1 (0.01)	2 (0.02)	3 (0.04)	9 (0.02)
Health	Male	4,295 (52.43)	5,703 (51.88)	5,634 (51.58)	4,272 (51.11)	4,369 (52.57)	24,273 (51.96)
	Female	3,896 (47.56)	5,289 (48.12)	5,232 (48.15)	4,086 (48.89)	3,942 (47.43)	22,445 (46.40)
	Total	8,191 (97.41)	10,992 (96.77)	10,866 (95.61)	8,358 (96.15)	8,311 (97.23)	46,718 (96.58)
Defects	Male	115 (52.5)	205 (55.86)	268 (53.771)	190 (56.72)	132 (55.70)	910 (54.95)
	Female	102 (46.79)	160 (43.60)	230 (46.09)	143 (42.69)	102 (43.04)	737 (44.50)
	Unknown	1 (0.46)	2 (0.54)	1 (0.20)	2 (0.06)	3 (1.26)	9 (0.54)
	Total	218 (2.59)	367 (3.23)	499 (4.39)	335 (3.85)	237 (2.77)	1,656 (3.42)

## Results

### Overall Prevalence of Birth Defects in Jiaxing, 2015–2019

Table 1 shows the overall prevalence of birth defects, including non-digestive in Jiaxing residents during the five-year period (2015–2019) covered by this study. Of the 48,374 participants, 1,656 cases had one or more congenital defects. The overall incidence of birth defects was 3.42%. Among the total subjects with birth defects there were 910 males (55.0%) and 737 females (44.5%), and 9 cases (0.5%) were indeterminate.

### Total Prevalence of Digestive Tract Defects in Jiaxing, 2015–2019

There was a total of 76 cases with digestive tract defects. The prevalence estimates per 10,000 births were as follows: 1.65 for esophageal atresia (8 cases); 1.24 for congenital defects of gastric musculature (6 cases); 2.33 for hypertrophic pyloric stenosis (2 cases) in 2019; 3.72 for duodenal and intestinal atresia (18 cases); 2.25 for congenital malrotation of intestine (9 cases) in 2016–2019; 1.45 for Hirschsprung's disease (6 cases); 4.75 for anal atresia/stricture (23 cases); and 1.40 for biliary atresia (4 cases) in 2017–2019 (Table 2).

### Gender Occurrence and Outcome of Digestive Tract Defects in Jiaxing, 2015–2019

Of the 76 cases with digestive tract malformations, 49 were male (60.5%) and 29 were female (38.2%), giving a male-to-female ratio of 1.58:1, and 1 case (1.3%) was indeterminable. The rate of death within 0–6 days was 9.2% (7 cases), while 22.4% (17 cases) were stillbirths, and 68.4% (52 cases) were live births (Table 3).

### Birth Weight and Gestational Age with Digestive Tract Defects in Jiaxing, 2015–2019

Table 4 showed the mean birth weight of the cases with digestive tract defects was  $2589.01 \pm 877.4$  (g). Eleven cases (14.5%) had a very low birth weight (<1500g), 20 cases (26.3%) had a low birth weight (1500~2499g), and 40.8% of cases had a low birth weight in this study. Moreover, the mean gestational age of the digestive tract defect cases was  $36.0 \pm 4.0$  weeks, which is below normal gestation ( $\geq 37$  weeks). There were 28 cases (36.8%) born at less than 37 weeks, and 48 cases (63.2%) were born at full-term. Among the total cases in our study, 25 (32.9%) had concomitant congenital heart disease.

## Discussion

At the present time, the incidence of congenital digestive tract defects among mainland Chinese people is rarely reported. Our study presents up-to-date figures for prevalence of congenital digestive tract defects in the population of Jiaxing City, China. In order to evaluate the incidence of digestive tract malformation in this region most accurately, our study is mainly based on analysis of the local registered population in a specific region. This study describes in a standardized way, a large number of cases with digestive tract malformation by

a total prevalence per 10,000 births. Our results showed that the overall incidence of birth defects was 3.42%. A study by Wang [26] reported that the incidence in Jiaxing was 2.1% between 2006 and 2010. The increase in the prevalence may be due to different registration methods during our study period.

Compared with other regions and countries, the incidence of congenital digestive tract defects in Jiaxing City of this study was different (Table 5). According to previous reports, the rates of esophageal atresia in Europe (2.23–2.57 per 10,000 births from 1987–2006; 2.56 per 10,000 births from 1980–1988) [27, 28] and Hawaii (2.2 per 10,000 births from 1989–2000) [29] were higher than in Jiaxing. The prevalence of hypertrophic pyloric stenosis in Taiwan Region (3.9 per 10,000 births from 1997–2007) [17] and in Sweden (8.5 per 10,000 births from 1987–1996) [30] was higher than in the present study. However, the data in our study included hypertrophic pyloric stenosis in only one year; this warrants further investigation in the future. A previous study showed that the incidence of duodenal atresia in England was 0.7–1.8 per 10,000 births [31]. Studies from Europe reported the overall incidence of Hirschsprung's disease in Europe was 1.03–1.05 per 10,000 births [5] and in England was 1.33–1.98 per 10,000 births [32]; these findings are similar to the prevalence in our study (1.45 per 10,000 births). The prevalence of anorectal atresia/stricture in a worldwide survey in 2006 (2.0–6.67 per 10,000 births) [33] and in Europe (4.05 per 10,000 births) [34] was also similar to our study. Previous studies reported that the incidence of biliary atresia in Taiwan Region was 0.89–1.90 per 10,000 births [35], in Japan was 0.96 per 10,000 births [36], and in Korea was 0.93–1.19 per 10,000 births [37], while in New York it was 0.76–0.93 per 10,000 births [38] and in overall USA it was 0.65–0.85 per 10,000 births [39]. The incidence in Jiaxing was similar to that in Taiwan Region. Several studies [35–37] have reported that biliary atresia is common in Asian countries, possibly attributed to racial and geographic factors. In addition, due to hypertrophic pyloric stenosis, Hirschsprung's disease and biliary atresia are usually detected more than seven days after birth, and data collected in this study cannot exclude the omission of the registration of birth defects. For example, some cases developed symptoms after the first seven days since birth, and attended other hospitals for treatment. However, compared with previous studies, the incidence in this study was within a reasonable range. Furthermore, the differences in incidence between previous reports from other countries and China may be attributable to racial, environmental, and genetic factors.

Of the 76 cases with congenital digestive tract defects in our study, 68.4% survived. Different digestive tract abnormalities may affect survival. The general consensus is that live-born cases with associated malformations may have higher rates of mortality [40, 41]; in our study, 32.9% also congenital heart disease, and this may be a risk factor that reduces survival. Additionally, the incidence of digestive tract

**Table 2:** Total prevalence of digestive tract defects in Jiaxing 2015-2019.

Category	Digestive tract defects	Rate per 10,000 births; 95% CI
2015	n=12	n=8,409
Esophageal atresia	1	1.19 (-)
Congenital defects of gastric musculature	0	-
Hypertrophic pyloric stenosis	0	-
Duodenal and intestinal atresia	3	3.57 (-)
Congenital malrotation of intestine	0	-
Hirschsprung's disease	1	1.19 (-)
Anal atresia/stricture	7	4.75 (1.3 to 12.2)
Biliary atresia	0	-
2016	n=13	n=11,359
Esophageal atresia	1	0.9 (-)
Congenital defects of gastric musculature	2	1.8 (-)
Hypertrophic pyloric stenosis	0	-
Duodenal and intestinal atresia	4	3.5 (-)
Congenital malrotation of intestine	4	3.5 (-)
Hirschsprung's disease	1	0.9 (-)
Anal atresia/stricture	1	0.9 (-)
Biliary atresia	0	-
2017	n=20	n=11,365
Esophageal atresia	2	1.76 (-)
Congenital defects of gastric musculature	0	-
Hypertrophic pyloric stenosis	0	-
Duodenal and intestinal atresia	5	4.40 (1.43 to 10.26)
Congenital malrotation of intestine	1	0.9 (-)
Hirschsprung's disease	1	0.9 (-)
Anal atresia/stricture	9	7.92 (3.62 to 15.03)
Biliary atresia	2	1.76 (-)
2018	n=17	n=8,693
Esophageal atresia	3	3.45 (-)
Congenital defects of gastric musculature	2	2.30 (-)
Hypertrophic pyloric stenosis	0	-
Duodenal and intestinal atresia	5	5.75 (1.87 to 13.42)
Congenital malrotation of intestine	1	1.1 (-)
Hirschsprung's disease	2	2.30 (-)
Anal atresia/stricture	3	3.45 (-)
Biliary atresia	1	1.1 (-)
2019	n=16	n=8,548
Esophageal atresia	1	1.16 (-)
Congenital defects of gastric musculature	2	2.33 (-)
Hypertrophic pyloric stenosis	2	2.33 (-)
Duodenal and intestinal atresia	1	1.16 (-)
Congenital malrotation of intestine	3	3.49 (-)
Hirschsprung's disease	1	1.16 (-)
Anal atresia/stricture	3	3.49 (-)
Biliary atresia	1	1.16 (-)
Total	n=76	n=48,374
Esophageal atresia	8	1.65 (-)
Congenital defects of gastric musculature	6	1.24 (-)
Hypertrophic pyloric stenosis <sup>a</sup>	2	2.33 (-)
Duodenal and intestinal atresia	18	3.72 (2.21-5.88)
Congenital malrotation of intestine <sup>b</sup>	9	2.25 (1.03-4.27)
Hirschsprung's disease	6	1.24 (-)
Anal atresia/stricture	23	4.75 (3.01-7.1)
Biliary atresia <sup>c</sup>	4	1.40 (-)

a: Per 10,000 births of 2019(total=8,548; total defects=237)

b: Per 10,000 births from 2016 and 2019(total=39,965; total defects=1,437)

c: Per 10,000 births from 2017 to 2019(total=28,606; total defects=1,071)

**Table 3:** Gender occurrence and outcome of digestive tract defects in Jiaying 2015-2019.

		Percentage		Birth Type	Cases	Percentage (%)
		Cases	(%)			
Esophageal atresia	Male	6	75.0	0 to 6 days of death	2	25.0
	Female	2	25.0	Stillbirth	1	12.5
				Survive	5	62.5
Congenital defects of gastric musculature	Male	4	66.7	0 to 6 days of death	-	-
	Female	2	33.3	Stillbirth	-	-
				Survive	6	100
Hypertrophic pyloric stenosis	Male	2	100	0 to 6 days of death		
	Female			Stillbirth		
				Survive	2	100
Duodenal and intestinal atresia	Male	6	36.8	0 to 6 days of death	1	
	Female	11	57.8	Stillbirth	6	
	Unknown	1	5.3	Survive	11	
Congenital malrotation of intestine	Male	6	66.7	0 to 6 days of death	-	-
	Female	3	33.3	Stillbirth	-	-
				Survive	9	100
Hirschsprung's disease	Male	4	66.7	0 to 6 days of death	-	-
	Female	2	33.3	Stillbirth	-	-
				Survive	6	100
Anal atresia/stricture	Male	15	65.2	0 to 6 days of death	4	17.4
	Female	8	34.8	Stillbirth	1	4.3
				Survive	18	78.3
Biliary atresia	Male	3	75.0	0 to 6 days of death	-	-
	Female	1	25.0	Stillbirth	-	-
				Survive	4	100
Total	Male	46	60.5	0 to 6 days of death	7	9.2
	Female	29	38.2	Stillbirth	17	22.4
	Unknown	1	1.3	Survive	52	68.4
	Male: Female		1.58:1			

**Table 4:** Birth weight and gestational age of the digestive tract defects in Jiaying 2015-2019.

	Cases n=76	Percentage %
Birth weight (2589.01±877.4) (g) ‡		
<1500	11	14.5
1500-2499	20	26.3
≥2500	45	59.2
Gestational age (36.0±4.0) (weeks) ‡		
<37	28	36.8
≥37	48	63.2
Congenital heart disease		
Yes	25	32.9
No	51	67.1

‡: Mean±SD

**Table 5:** Incidence and category of digestive tract defects in different regions.

Category	Area	Survey Year	Incidence
			(per 10,000 births)
Esophageal atresia	Jiaying, China	2015–2019	1.65
	Europe	1987–2006	2.43 (2.23–2.57) (Pedersen, et al., 2012)
	Europe	1980–1988	2.86 (Depaepe, et al., 1993)
	Hawaii	1989–2000	2.2 (Forrester & Merz, 2005)
Hypertrophic pyloric stenosis	Jiaying, China	2019	2.14
	Taiwan Region	1997–2007	3.9 (3.0–4.7) (Leong, et al., 2007)
	Sweden	1987–1996	8.5 (Hedback, 2001)
Duodenal and intestinal atresia	Jiaying, China	2015–2019	3.72
	England	1991–2001	0.7–1.8 (Best, et al., 2012)
Hirschsprung's disease	Jiaying, China	2015–2019	2.14
	Europe	2012	1.09 (1.03–1.15) (Best, et al., 2014)
	England	1990–2008	1.63 (1.33–1.98) (International clearinghouse birth defect surveillance and research. Annual report, 2008)
Anal atresia/stricture	Jiaying, China	2015–2019	4.75
	Europe	1980–1994	4.05 (Cuschieri, 2010)
	Worldwide	2006	2.0–6.67 (Tiao, et al., 2008)
Biliary atresia	Jiaying, China	2017–2019	1.4
	Taiwan Region	1996–2003	1.46 (0.89–1.90) (Tiao, et al., 2008)
	Japan	1989–1999	0.96 (Nio, et al., 2003)
	Korea	2011–2015	1.06 (0.93–1.19) (Lee, et al., 2017)
	New York	1983–1998	0.85 (0.76–0.93) (Caton, et al., 2004)
	USA	1997–2000	0.65–0.85 (Shneider, et al., 2006)

malformations in male infants was higher than in female infants (male: female=1.58:1), which was consistent with previous studies [42-44]. Compared with other congenital malformations, digestive tract defects are not easily detected immediately after birth, especially biliary atresia. In addition, the general population know little about congenital digestive tract defects, and it is necessary to educate patients about these diseases during the perinatal period and establish targeted prevention and awareness programs to prompt faster diagnosis and expedite treatment.

In the current study, although the association between preterm birth and congenital alimentary tract malformation was not assessed, more than a third of cases (39.2%) were premature births. Other studies have reported similar results.

For example, a study of esophageal atresia in 23 European regions found that one third of live-born infants with isolated esophageal atresia were born preterm (gestational age <37 weeks) [28], and this was also demonstrated in a study regarding isolated anal anomalies [43]. Some studies have also reported that low birth weight is associated with higher incidence of birth defects. Yoon et al. [44] found that the incidence of biliary atresia in infants weighing less than 2500g was higher than in infants of normal weight, and considered that low birth weight was an independent risk factor for biliary atresia. Digestive tract malformation will undoubtedly affect the normal function of a newborn's digestive system, thereby hindering children's digestion and absorption of nutrients. In tandem with these findings, our study showed that more than a third (40.8%) of the

gastrointestinal malformation cases had lower birth weight than normal newborns. Most newborns with low birth weight are premature infants. Premature birth and low birth weight may be risk factors for the occurrence of digestive tract malformations. However, these findings require further investigation and research.

Our study had some limitations. Firstly, the database only covered a five-year period (2015–2019) of birth registration, meaning that our investigation utilized relatively short-term data. Secondly, newborn data in this study was not linked to maternal data, so it was not possible to consider or adjust for confounding factors such as perinatal health. In addition, congenital digestive tract defects are not easily diagnosed within seven days of birth, particularly hypertrophic pyloric stenosis, Hirschsprung's disease, and biliary atresia. Therefore, there may have been omissions in the registration of birth defects in our study and some inaccuracy in the incidence estimates for biliary atresia. However, a major strength of this study was based on the population of a region in mainland China. The estimated incidence of congenital digestive tract malformations in mainland China is based upon studies that have been published abroad. There is little to no local information on this subject specific to China, and we believe more accurate local data will assist clinicians, researchers, and healthcare planners in providing better diagnostic and prognostic outcomes for newborns and their families by establishing awareness programs and increasing and expediting diagnosis and treatment. Our findings point out that digestive tract defects are not always established immediately after birth, which naturally impacts upon the health of the newborn, and these findings support and are supported by the findings of numerous other studies published throughout the world, though none relate to China at the same level of specificity as this study. In addition, we found that roughly one third of our subjects with digestive tract defects also had concomitant congenital heart disease, suggesting a link between the two which may warrant further investigation. China is a vast territory with a large and fluid population base, so it is difficult to compile very large sample reports focusing on digestive tract malformations. Thus, so far the prevalence of congenital digestive tract defects among Chinese people is rarely reported. This study fills a gap in the incidence of digestive tract malformations.

## Conclusion

The focus on digestive tract defects in the present report, using data from Jiaying, China (2015–2019), is intended to provide more detailed information on the occurrence of these rare birth defects. This study estimated the incidence of digestive tract malformations, and the findings may provide a useful foundation for future epidemiologic studies of these congenital diseases. Moreover, our data will also be helpful in determining the resources needed for

basic and public health research into digestive tract malformation in China.

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