Original Article

Rising Birth Prevalence of Gastroschisis

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OBJECTIVE:
Gastroschisis is a congenital anomaly that has been reported to be increasing in frequency. The objective of this study was to determine the birth prevalence of gastroschisis using two large databases.

STUDY DESIGN:
We reviewed data from a statewide database and a national database from a neonatal health care provider, abstracting cases of gastroschisis.

RESULTS:
In North Carolina, the birth prevalence of gastroschisis increased from 1.96 per 10,000 births in 1997 to 4.49 per 10,000 births in 2000 ($p = 0.0007$). The overall increase was almost entirely because of the increase in infants born to mothers less than 20 years old. Among infants receiving care from the national neonatal provider, the prevalence of gastroschisis increased from 2.9 per 1000 patients in 1997 to five per 1000 patients in 2001 ($p = 0.044$).

CONCLUSION:
The birth prevalence of gastroschisis is increasing in North Carolina, and this trend may be occurring nationally. The rapid change in the birth prevalence in the subset of population most at risk for gastroschisis implicates environmental or pharmacologic teratogens rather than changing population characteristics as a causal factor in the development of gastroschisis.
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INTRODUCTION

Gastroschisis is a rare congenital malformation of the abdominal wall associated with significant neonatal mortality and morbidity. The mortality rate for gastroschisis is reported to approach 10%.[1,2] Despite surgical correction, morbidities, include feeding intolerance, failure to thrive, and prolonged duration of hospitalization in nearly all infants with this anomaly.[3]

Several studies have reported increases in the birth prevalence of gastroschisis in recent decades. These studies have based conclusions on a small number of reported cases,[4–6] or relied on hospital self-reporting using a survey tool with less than optimal response.[7] A recent study from Denmark reported no significant increase in the birth prevalence of gastroschisis over a 20 year period.[8] The single investigation of this question in a statewide population of infants in the United States reported a modest increase between 1986 and 1997.[9]

In this study, we sought to investigate changes in the birth prevalence of gastroschisis using data from a population-based state registry and data from a consortium of neonatal practices representing infants from across the United States.

MATERIALS AND METHODS

We identified infants with gastroschisis born between 1/1/1997 and 12/31/2000 from the registry of the North Carolina Birth Defects Monitoring Program (NCBDMP). The NCBDMP is a population-based surveillance system that collects data on congenital malformations diagnosed within the first year of life among all live births in North Carolina. To identify cases, we searched the database using the Centers for Disease Control and Prevention modified British Pediatric Association code 756.710, that is specific to gastroschisis. To verify inclusion of all cases, infants with gastroschisis were also identified by reviewing hospital disease indexes of North Carolina's 12 tertiary neonatal care centers and genetics and prenatal diagnosis reporting logs in selected centers. Trained case abstractors reviewed the medical records at the tertiary neonatal care centers to confirm the diagnosis of gastroschisis.

We also reviewed data recorded in a database maintained by a national consortium of neonatal health care providers (Pediatrix Medical Group, Inc., Sunshine, FL). The database is formed from a computer-assisted tool that generates hospital admission, daily progress, and discharge notes for the neonatal intensive care units in the consortium. Infants with gastroschisis were identified among all infants admitted to participating units between 1/1/1997 and 12/31/2001. To control for ascertainment

bias as a result of the recruitment of new centers, the birth prevalence of omphalocele was calculated to provide an internal comparison to another anomaly requiring pediatric surgical intervention. Duplicate entries resulting from transfer between consortium units were excluded.

A Poisson log-linear model was fitted to the data from both sources using SAS PROC GENMOD (SAS Institute, Cary, NC), modeling the change in rates as a function of year.

RESULTS

The birth prevalence of gastroschisis in North Carolina increased from 1.96 cases per 10,000 births in 1997 to 4.49 in 2000 ($p = 0.0007$; Table 1). There was a large change in the birth prevalence for mothers less than 20 from 1997 to 2000 (3.26 per 10,000 births to 15.31; Table 2), which accounts for most of the overall increase of birth prevalence of gastroschisis. The maternal demographics for all births did not change from 1997 to 2000 (Table 3).

Table 1 Birth Prevalence Rates for Gastroschisis in North Carolina

	1997	1998	1999	2000
Number of births	106,949	111,631	113,755	120,247
Number of cases of gastroschisis	21	33	41	54
Number of cases per 10,000 births	1.96	2.96	3.6	4.49

Table 2 Maternal Demographics of Infants with Gastroschisis in North Carolina, Number of Cases Per 10,000 Births

Age in years	1997	1998	1999	2000
<20	3.26	13.42	10.4	15.31
20–24	3.80	2.63	5.13	4.84
25–29	1.00	0.65	1.89	2.73
>29	0.30	0.58	0.85	1.30

Table 3 Maternal Demographics for All Births in North Carolina

	1997	1998	1999	2000
Age in years				
<20, *n* (%)	15,350 (14)	15,653 (14)	15,390 (14)	15,678 (13)
20–24, *n* (%)	28,937 (27)	30,372 (27)	31,215 (27)	33,030 (27)
25–29, *n* (%)	29,851 (28)	30,870 (28)	31,720 (28)	32,975 (27)
>29, *n* (%)	32,810 (31)	34,733 (31)	35,424 (31)	38,560 (32)
Ethnicity				
Black, *n* (%)	27,356 (26)	28,133 (25)	28,277 (25)	29,206 (24)
Hispanic, *n* (%)	6812 (6)	8033 (7)	9784 (9)	12,470 (10)
White, *n* (%)	69,073 (65)	71,290 (64)	71,500 (63)	74,001 (62)
Other, *n* (%)	3708 (4)	4175 (4)	4194 (4)	4570 (4)

The incidence of gastroschisis in the national neonatal practice consortium increased from 2.9 per 1000 admitted patients in 1997 to five in 2001 ($p = 0.0044$; Table 4). Again, there was a large change in the incidence of gastroschisis for younger mothers from 1997 to 2001 (Table 5). There was no change in the incidence of omphalocele (Table 4). The mothers of neonates with gastroschisis (22±5) were younger than mothers of neonates without gastroschisis (28±6) and mothers of neonates with omphalocele (28±6, $p<0.05$). The maternal demographics for all admissions into the national consortium of neonatal units did not change (Table 6).

SIGNIFICANCE

The birth prevalence of gastroschisis increased in North Carolina by approximately 130% between 1997 and 2000. A strong inverse relation between maternal age and gastroschisis has been reported previously,[6] and our study confirms that maternal age less than 20 is a risk factor. Most importantly, we have demonstrated a large increase in the birth prevalence in the population that is already most at risk. The change in birth prevalence during the study period is due primarily to an increase among teen mothers.

Table 4 Incidence Rates for Gastroschisis in the National Consortium of Neonatal Units

	1997	1998	1999	2000	2001
Number of patients	10,342	7,676	25,091	32,784	35,881
Number of cases of gastroschisis	30	73	100	149	178
Number of cases per 1000 patients	2.9	4.1	4.0	4.5	5.0
Number of cases of omphalocele	18	33	50	68	62
Number of cases per 1000 patients	1.7	1.9	2.0	2.1	1.7

Table 5 Maternal Demographics of Infants with Gastroschisis from National Consortium of Neonatal Units, Number of Cases Per 1000 Patients

Age in years	1997	1998	1999	2000	2001
<20	8.2	12.1	13.7	16.0	18.0
20–24	3.6	6.5	5.0	7.5	8.1
25–29	3.1	3.8	2.2	3.0	2.7
>29	0.8	0.7	1.5	0.6	1.2

Table 6 Maternal Demographics for all Admissions in National Consortium of Neonatal Units

	1997	1998	1999	2000	2001
Age in years					
<20, *n* (%)	1093 (12)	1813 (13)	2409 (12)	3056 (12)	3328 (12)
20–24, *n* (%)	1939 (22)	3232 (23)	4405 (23)	5769 (23)	6414 (23)
25–29, *n* (%)	2239 (25)	3692 (26)	5003 (26)	6322 (26)	6777 (25)
>0, *n* (%)	3655 (41)	5520 (38)	7496 (39)	9648 (39)	11,089 (40)
Ethnicity					
Black, *n* (%)	1834 (18)	2770 (16)	3451 (14)	4564 (14)	4969 (14)
Hispanic, *n* (%)	1715 (17)	3428 (19)	5385 (22)	6931 (21)	8101 (23)
White, *n* (%)	5395 (52)	9673 (55)	13,760 (55)	18,024 (55)	19,328 (54)
Other, *n* (%)	512 (12)	917 (8)	1373 (8)	1838 (8)	1980 (7)

A similar overall increase was also observed among infants receiving care from a national consortium of neonatal units, without a change in maternal demographics. The patient population receiving care from the consortium changed during the period of observation, evidenced by a tripling of the number of admissions to participating units. However, it is doubtful that infants with abdominal wall defects increased disproportionately in recent years, as this would have been reflected in an increased incidence of omphalocele, whose incidence did not change during the study period. Therefore, it is possible that an increase in the birth prevalence of gastroschisis is a national phenomenon.

Similar trends have been observed in the United Kingdom, Japan, and Australia. However, in North Carolina the birth prevalence is higher and the rapidity and the magnitude of the increase in birth prevalence were greater. The difference between our study and previous reports may have resulted from observations made during a more recent period of time in our study, or they may reflect differences in the demographics or genetic pools of the study population.

We theorize that the rapid increase of the birth prevalence of gastroschisis in a specific population can be explained on the basis of an exposure to an environmental factor. Candidate factors might include illicit drugs such as ''ecstasy'' or other methamphetamines, over-the-counter medications, dietary changes, or food additives. The maternal use of a variety of medications, including pseudoephedrine, phenylpropranolamine, aspirin, ibuprofen, and acetaminophen, has been associated with an increased risk of gastroschisis.[10–13] Additional risk may occur when combinations of these medications are used.[14] Torfs et al.[15] demonstrated that teenage diets, with lower intake of α-carotene, total glutathione, and high levels of nitrosamines, were associated with increased risk of gastroschisis.

In conclusion, the birth prevalence of gastroschisis in North Carolina, and perhaps in the United States, is increasing. Owing to the significant morbidity and mortality associated with this anomaly, a detailed investigation of potential risk factors and teratogens should be undertaken.

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