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Prevalence and Correlates of Gastroschisis in 15 States, 1995 to 2005

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Abstract

OBJECTIVE—To identify trends in the prevalence and epidemiologic correlates of gastroschisis using a large population-based sample with cases identified by the National Birth Defects Prevention Network over the course of an 11-year period.

METHODS—This study examined 4,713 cases of gastroschisis occurring in 15 states during 1995–2005, using public use natality data sets for denominators. Multivariable Poisson regression was used to identify statistically significant risk factors, and Joinpoint regression analyses were conducted to assess temporal trends in gastroschisis prevalence by maternal age and race and ethnicity.

RESULTS—Results show an increasing temporal trend for gastroschisis (from 2.32 per 10,000 to 4.42 per 10,000 live births). Increasing prevalence of gastroschisis has occurred primarily among younger mothers (11.45 per 10,000 live births among mothers younger than age 20 years compared with 5.35 per 10,000 among women aged 20 to 24 years). In the multivariable analysis,

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using non-Hispanic whites as the referent group, non-Hispanic black women had the lowest risk of having a gastroschisis-affected pregnancy (prevalence ratio 0.42, 95% confidence interval [CI] 0.37–0.48), followed by Hispanics (prevalence ratio 0.86, 95% CI 0.81–0.92). Gastroschisis prevalence did not differ by newborn sex.

CONCLUSIONS—Our findings demonstrate that the prevalence of gastroschisis has been increasing since 1995 among 15 states in the United States, and that higher rates of gastroschisis are associated with non-Hispanic white maternal race and ethnicity, and maternal age younger than 25 years (particularly younger than 20 years of age).

Gastroschisis, a congenital malformation causing the herniation of intestines and other abdominal organs outside of the fetal abdominal wall, continues to capture the attention of epidemiologists because of ongoing reports of the as-yet-unexplained increase in prevalence. Gastroschisis typically results in term or near-term live birth, with few comorbid congenital disorders.[1–4] Whereas the cause of gastroschisis is unknown, identified risk factors include young maternal age with a lower body mass index (calculated as weight (kg)/[height (m)]^2)[5] and maternal race and ethnicity.[6–8] Compared with foreign-born mothers, mothers born in the United States have a higher risk of having a neonate born with gastroschisis.[9]

Whereas estimates of prevalence of gastroschisis range from 2 to 3 cases per 10,000 live births, numerous reports indicate an increasing prevalence both in the United States and worldwide.[1,8,10–15] Previous United States studies evaluating the trends and correlates of gastroschisis have been limited by the relatively rare occurrence. Small case counts may have prevented recognition of social, demographic, and clinical factors that might have provided information for prevention or intervention efforts. We therefore leveraged interstate collaboration within the National Birth Defects Prevention Network to pool data from a large, population-based, and nationally representative sample of gastroschisis cases over the course of 11 years to address the following research questions: What is the prevalence of gastroschisis in the United States?; Is there evidence to show that the prevalence has been increasing in the past two decades?; Are there subgroups of women at higher risk for having a neonate born with gastroschisis (eg, maternal age, racial, or ethnic groups)?; and Are there demographic (eg, sex of the newborn) or reproductive (eg, multiple gestations) characteristics associated with the occurrence of gastroschisis?

MATERIALS AND METHODS

This study assessed the prevalence of gastroschisis in 15 states from 1995 to 2005. We invited all states with population-based birth defects registries to participate in this project. Our only requirements were that they have continuous data from 2005 backward to whatever full calendar year was the earliest they could contribute, and that the gastroschisis and omphalocele diagnoses were clinically confirmed by medical chart review. Several states could not meet these criteria, including large states that relied primarily on hospital discharge records with no case confirmation (eg, Illinois, Michigan) and others that for administrative reasons did not wish to participate (eg, Hawaii). Massachusetts did not have enough years under surveillance. Two states (New Mexico and Washington) were so interested in participating that they conducted special projects using active surveillance only for gastroschisis cases from 1999 to 2005 so their data could be included in this project.

Participating states included Arizona, Arkansas, California (select counties), Colorado, Georgia (select counties), Iowa, Kentucky, New Mexico, New York, Oklahoma, North Carolina, Rhode Island, Texas, Utah, and Washington. All states operated population-based birth defects surveillance programs that included gastroschisis in its case definition and were willing to provide access to de-identified, individual-level case data. In Georgia and California, the programs ascertain all birth defects occurring in women residing in catchment areas of contiguous counties. Although states incorporated various case ascertainment strategies along the continuum from passive to active surveillance, those programs that used passive case-finding strategies performed clinical chart reviews by medical personnel to confirm the gastroschisis diagnosis and to differentiate these cases from cases of omphalocele. Demographic and perinatal data, including maternal age, maternal race and ethnicity, plurality, and sex of the newborn, were obtained for the entire study population. Maternal age was categorized into younger than 20 years, 20–24 years, 25–29 years, 30–34 years, or 35 years and older. Maternal race and ethnicity were determined based on maternal self-report and was first grouped by ethnicity (Hispanic or non-Hispanic), with the non-Hispanic group further subdivided by race (white, black, Native American, Asian or Pacific Islander, and other). Fetal number was grouped into singleton and multiple gestation (twins and higher-order) categories.

Birth prevalence of gastroschisis was calculated for each year, state, and category of maternal age, race and ethnicity, sex of the newborn, and plurality (fetal number). Cases (numerator) consisted of all birth outcomes affected by gastroschisis, including live born neonates, fetal deaths, and elective terminations. Population data were based exclusively on the total number of live births and were obtained primarily from the National Center on Health Statistics. In some instances (California, 1995–2005; Texas 1996–1998), population data were obtained from the Office of Vital Statistics of the state. Birth prevalence was calculated as the number of gastroschisis cases (of any birth outcome) divided by the total number of live births. Live births are used as the denominator; because the true number of spontaneous fetal deaths and pregnancy terminations are relatively small in comparison with all births, the absence of fetal deaths in the denominator has relatively little effect on the final prevalence estimate. Poisson regression was used to generate 95% confidence intervals (CIs) for each birth prevalence estimate and to calculate crude prevalence ratios and 95% CIs for each covariate (maternal age, maternal race and ethnicity, plurality, and sex of the newborn) adjusted for state of residence. A multivariable Poisson regression model with all covariates included was used to estimate adjusted prevalence ratios and 95% CIs. To test for a linear trend in the gastroschisis prevalence over the course of the study period, we included year of delivery as a continuous covariate in the adjusted model. Multivariable analyses were initially conducted using an “era” variable to divide the study period into the periods 1995–2000 and 2001–2005, but this variable did not contribute to the adjusted model and was not included in our final models.

Joinpoint regression analysis was used to identify statistically significant temporal trends of gastroschisis prevalence by maternal age and race and ethnicity.[16] First, annual trend data are modeled by fitting a straight line (ie, zero joinpoints). Next, a model with one joinpoint is compared with the null using a Monte Carlo permutation test and, if so, the joinpoint is incorporated into the model. An iterative process ensues, and additional joinpoints are considered in the same manner until an optimal-fitting model is selected. Each joinpoint represents a statistically significant change (increasing or decreasing) in the temporal trend of gastroschisis rates, and an annual percent change and its 95% CI are calculated to describe how the rate changes within each time interval. We excluded the "other" race category from our joinpoint regression models because there were too few cases to allow for a reliable trend analysis.

All statistical tests were two-sided and declared significant at P<.05. Most statistical analyses were performed with SAS software 9.2; however, Joinpoint analyses were performed using the Joinpoint Regression Program (3.5.4). Approval for the study was obtained from the Institutional Review Board at the University of South Florida.

RESULTS

From 1995 to 2005, there were 13,233,776 live births and 4,713 gastroschisis cases among the 15 participating states (birth prevalence 3.56 per 10,000 live births). A consistent increase in the rate of gastroschisis was noted during the study period, from 2.32 per 10,000 in 1995 to 4.42 per 10,000 in 2005 (P_{trend} <.001; Table 1). Joinpoint regression confirmed that a single linear trend provided the best fit to the annual prevalence data. The prevalence of gastroschisis for each participating state is presented in Table 2. The lowest rate was reported by New York (1.53), and Arkansas had the highest rate of gastroschisis (5.06). Differences in prevalence rates between states did not appear to vary consistently based on race or ethnicity (data not shown).

The distributions of the study population, birth prevalence, and prevalence ratios for gastroschisis by selected maternal and neonate characteristics are presented in Table 3. Women younger than 20 years of age had the highest prevalence rate of gastroschisis. Among maternal racial and ethnic groupings, mothers reporting "other" race or ethnicity had the highest rate of neonates born with gastroschisis (5.47), followed by Native Americans (5.48), Hispanics (4.06), and non-Hispanic whites (3.50). Asian or Pacific Islanders and non-Hispanic blacks had the lowest rates, 2.20 and 2.25, respectively.

After multivariable analyses adjusting for state of residence (Table 3), women younger than age 20 years were 7.2-times more likely to have an offspring with gastroschisis compared with women 25–29 years of age (prevalence ratio, 7.18, 95% CI 6.51–7.92), and women 20–24 years of age were three-times more likely to deliver a newborn with gastroschisis (prevalence ratio 3.25, 95% CI 2.95–3.58). As maternal age increased, the risk of gastroschisis gradually declined. Compared with non-Hispanic whites, non-Hispanic black women had the lowest risk of having a gastroschisis-affected pregnancy (prevalence ratio 0.42, 95% CI 0.37–0.48), followed by His-panics (prevalence ratio 0.86, 95% CI 0.81–0.92). Compared with singleton pregnancies, multiple gestation pregnancies were less likely to be affected by gastroschisis (prevalence ratio 0.76, 95% CI 0.60–0.98). Prevalence did not vary by newborn sex.

Trends in gastroschisis prevalence rates and the results of the Joinpoint analysis by maternal age group and maternal race and ethnicity are shown in Figures 1 and 2. Statistically significant increases in gastroschisis prevalence rates between 1995 and 2005 were seen for all maternal age groups younger than 30 years, but not for those 30 years of age and older (Fig. 1). Trends also increased significantly for non-Hispanic whites, non-Hispanic blacks, and His-panics (Fig. 2). Although not statistically significant, slight increases in prevalence rates for Asian or Pacific Islanders and Native Americans were present.

DISCUSSION

In this large population-based study, we addressed three research questions. Our study demonstrates a consistent increasing trend in the birth prevalence of gastroschisis in the United States during the period 1995–2005. We also confirm a strong inverse association of gastroschisis with maternal age and with multiple gestation pregnancy. Crude prevalence ratios differed for all racial and ethnic groups analyzed, with lower prevalence among non-Hispanic black and Asian or Pacific Islanders compared with non-His-panic whites. However, after adjustment for maternal age, multiple gestation, and sex of the newborn, differences by race and ethnicity were observed only for non-Hispanic black and Hispanic mothers compared with non-Hispanic whites.

Our findings support previous findings put forward by several other investigators[1,8,11,13,14] indicating that the prevalence of gastroschisis has been increasing during the past two decades in the United States. Consistent with other reports,[5–9] this large study also identified the maternal risk factors of non-Hispanic ethnicity and white race and age younger than 25 years (and particularly younger than age 20 years) were associated with higher rates of gastroschisis.

Researchers have offered several hypotheses to explain the increasing prevalence of gastroschisis in the United States and around the world. Although recreational drug use has been proposed as a potential risk factor,[17,18] the evidence for this association is limited and seems unlikely to account for much of the observed increase in prevalence. Similarly, Werler et al[19] considered the role of vasoactive medication and Browne et al[20] examined caffeine intake and found inconsistent evidence in support of the vascular disruption hypothesis. Gastroschisis also has been the focus of numerous public health cluster investigations, but to date these studies have not yielded insights into risk factors that are major drivers of the observed increasing trend.[17,21]

The primary strengths of this study are the size and breadth of the sample. This large United States study includes more than 13 million live births, comprising more than one-third of all United States births for most years studied, with data from 15 states generally representative of the national population and including considerable racial and ethnic diversity. Data regarding gastroschisis cases were obtained from population-based surveillance programs in each state, in contrast to clinical studies based on pediatric surgery networks.[22] Limitations include fewer states participating in the years before 1999, as well as some variability in case ascertainment methods. Some states provided data for all cases, including stillbirths and terminations, whereas all provided data for cases among live born neonates. We conducted sensitivity analyses restricted to years during which all states participated (1999–2005) and did not observe significant differences from our findings covering the entire study period.

Although every effort was made to identify and exclude cases of amniotic band syndrome and limb-body-wall complex, it is possible that a few of these cases were included as gastroschisis cases in this study. However, we estimate the number to be less than 1% of all cases, so the effect, if any, on our results should be minimal. Although this report includes all cases, restricting the analyses to cases among live births did not substantially change the statistical findings. Because of inconsistencies in data from several states that resulted in large numbers of records with missing data, maternal smoking during pregnancy and parity were not examined. With the increasing use of the 2003 revision of the national certificates of live birth and fetal death,[23] maternal prepregnancy body mass index will become available for population-based analysis. Unfortunately, these data elements were not sufficiently in use to be included in this study. Future analyses of these data will focus on the roles of nativity, birth weight, gestational age, multiple anomalies, and survival patterns.

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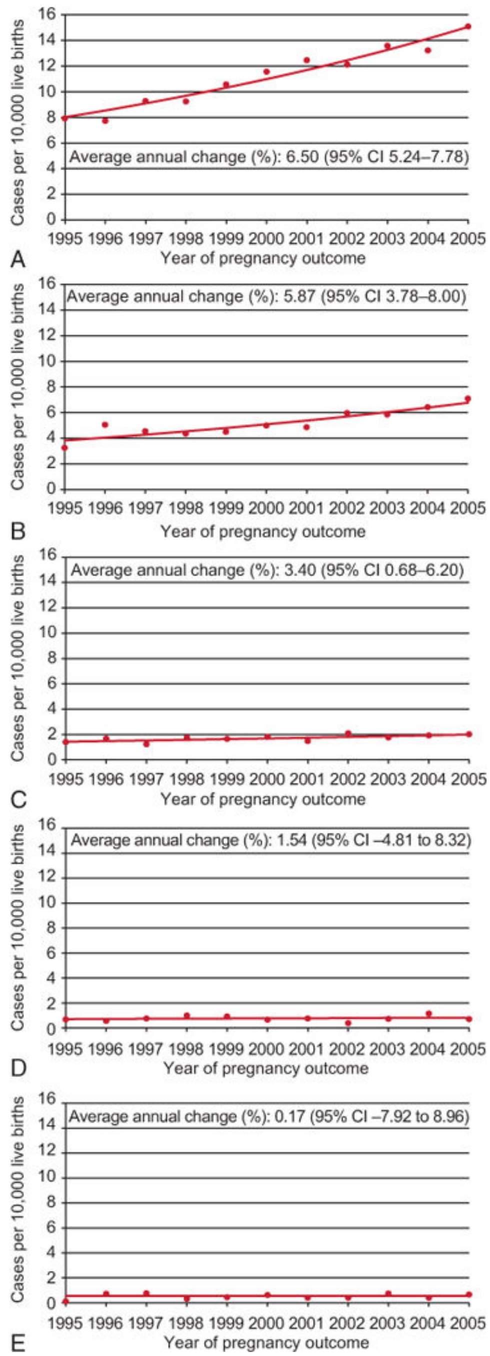

Fig. 1.

Trends in gastroschisis prevalence by maternal age group from 1995 to 2005. Note that the average annual change (%) is a point estimate. **A.** Younger than 20 years of age. **B.** Age 20–24 years. **C.** Age 25–29 years. **D.** Age 30–34 years. **E.** Age 35 years or older. CI, confidence interval.

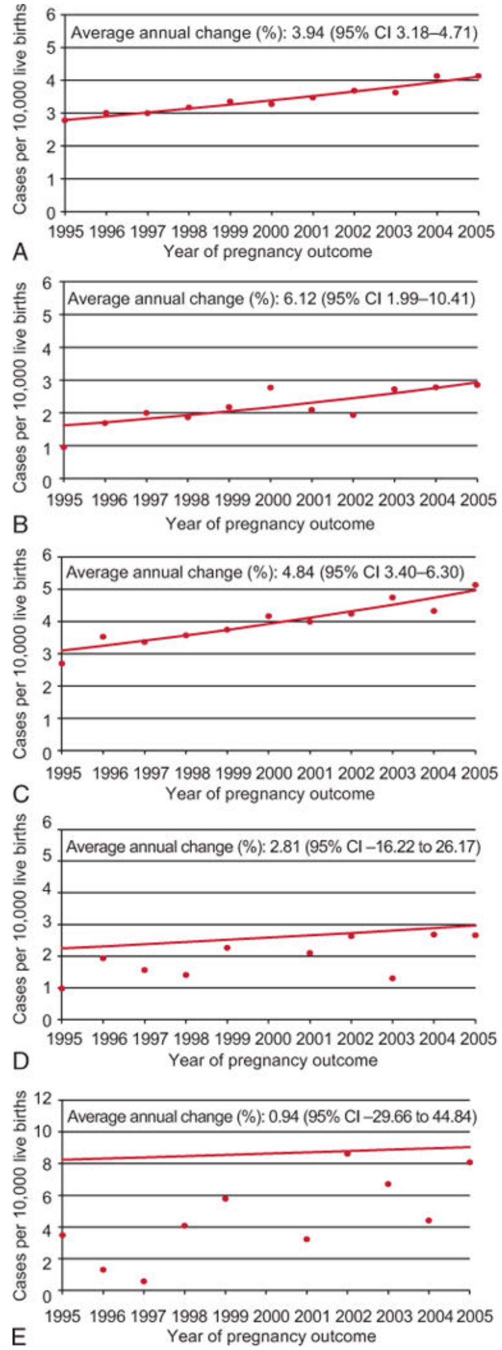

Fig. 2.

Trends in gastroschisis prevalence by maternal race and ethnicity from 1995 to 2005. Note that the average annual change (%) is a point estimate. **A.** Non-Hispanic white. **B.** Non-Hispanic black. **C.** Hispanic. **D.** Asian or Pacific Islander. **E.** American Indian or Alaskan Native. Please note a different y-axis scale for the American Indian or Alaskan Native group. CI, confidence interval.

Table 1

Annual Prevalence of Gastroschisis in Selected States in the United States, 1995 to 2005*

Year Crude	Cases	Total Live Births	Prevalence Rate† (95% CI)	Prevalence Ratio (95% CI)
1995	173	746,781	2.32 (2.00–2.69)	0.69 (0.58–0.82)
1996	251	851,010	2.95 (2.61–3.34)	0.88 (0.75–1.03)
1997	300	1,010,914	2.97 (2.65–3.32)	0.88 (0.76–1.02)
1998	320	1,015,115	3.15 (2.83–3.52)	0.94 (0.81–1.08)
1999	439	1,307,733	3.36 (3.06–3.69)	Reference
2000	489	1,351,074	3.62 (3.31–3.95)	1.08 (0.95–1.23)
2001	492	1,385,485	3.55 (3.25–3.88)	1.06 (0.93–1.20)
2002	525	1,396,345	3.76 (3.45–4.10)	1.12 (0.99–1.27)
2003	539	1,377,989	3.91 (3.59–4.26)	1.17 (1.03–1.32)
2004	564	1,387,787	4.06 (3.74–4.41)	1.21 (1.07–1.37)
2005	621	1,403,543	4.42 (4.09–4.79)	1.32 (1.17–1.49)
Total	4,713	13,233,776	3.56 (3.46–3.66)	

CI, confidence interval.

*States include Arizona, Arkansas, California, Colorado, Georgia, Iowa, Kentucky, New Mexico, New York, Oklahoma, North Carolina, Rhode Island, Texas, Utah, and Washington. 1995 does not include Arkansas, Colorado, Kentucky, North Carolina, New Mexico, Texas, Utah, Washington; 1996 does not include Arkansas, Colorado, Kentucky, North Carolina, New Mexico, Utah, Washington; 1997 does not include Arkansas, Kentucky, North Carolina, New Mexico, Washington; and 1998 does not include Arkansas, North Carolina, and Washington. Data for California and Georgia are for selected counties only.

†Gastroschisis cases per 10,000 live births.

Table 2

Prevalence of Gastroschisis by State From 1995 to 2005*

State	Years	Cases	Total Live Births	Prevalence Rate† (95% CI)	Crude Prevalence Ratio (95% CI)
Arkansas	1999–2005	134	264,524	5.06 (4.28–6.00)	3.31 (2.72–4.01)
Oklahoma	1995–2005	267	542,980	4.91 (4.36–5.54)	3.21 (2.76–3.74)
Kentucky	1998–2005	207	441,052	4.69 (4.10–5.38)	3.06 (2.60–3.62)
New Mexico	1998–2005	101	221,653	4.55 (3.75–5.54)	2.98 (2.40–3.69)
Iowa	1995–2005	186	414,815	4.48 (3.88–5.18)	2.93 (2.47–3.48)
Utah	1997–2005	191	431,094	4.43 (3.84–5.11)	2.89 (2.44–3.43)
Texas	1996–2005	1,344	3,187,814	4.21 (4.00–4.45)	2.75 (2.47–3.07)
Arizona	1995–2005	388	922,408	4.20 (3.81–4.65)	2.75 (2.39–3.15)
Colorado	1997–2005	236	585,926	4.03 (3.55–4.58)	2.63 (2.24–3.08)
California	1995–2005	526	1,341,693	3.92 (3.60–4.27)	2.56 (2.25–2.91)
North Carolina	1999–2005	322	830,892	3.87 (3.47–4.32)	2.53 (2.19–2.92)
Washington	1999–2005	200	564,159	3.54 (3.09–4.07)	2.31 (1.96–2.74)
Rhode Island	1995–2005	49	139,645	3.51 (2.65–4.64)	2.29 (1.70–3.08)
Georgia	1995–2005	130	524,542	2.48 (2.09–2.94)	1.62 (1.33–1.97)
New York	1995–2005	432	2,820,579	1.53 (1.39–1.68)	Reference

CI, confidence interval.

States are ordered by decreasing prevalence rate.

*States include Arizona, Arkansas, California, Colorado, Georgia, Iowa, Kentucky, New Mexico, New York, Oklahoma, North Carolina, Rhode Island, Texas, Utah, and Washington. 1995 does not include Arkansas, Colorado, Kentucky, North Carolina, New Mexico, Texas, Utah, Washington; 1996 does not include Arkansas, Colorado, Kentucky, North Carolina, New Mexico, Utah, Washington; 1997 does not include Arkansas, Kentucky, North Carolina, New Mexico, Washington; and 1998 does not include Arkansas, North Carolina, and Washington. Data for California and Georgia are for selected counties only.

†Gastroschisis cases per 10,000 live births.

Table 3

Prevalence Rates and Ratios of Gastroschisis by Maternal and Newborn Characteristics in Selected States in the United States From 1995 to 2005*

Characteristic	Cases†	Total Live Births†	Prevalence Rate (95% CI)‡	Crude Prevalence Ratio (95% CI)	Adjusted Prevalence Ratio (95% CI)§
Maternal age (y)					
Younger than 20	1,822	1,589,319	11.45 (10.95–12.00)	6.69 (6.10–7.33)	6.99 (6.34–7.71)
20–24	1,835	3,430,636	5.35 (5.11–5.60)	3.12 (2.85–3.42)	3.19 (2.89–3.52)
25–29	612	3,571,446	1.71 (1.58–1.85)	Reference	Reference
30–34	218	2,943,860	0.74 (0.65–0.85)	0.43 (0.37–0.50)	0.44 (0.37–0.51)
35 and older	86	1,697,974	0.51 (0.41–0.63)	0.30 (0.24–0.37)	0.29 (0.23–0.37)
Maternal race and ethnicity					
White non-Hispanic	2,321	6,635,528	3.50 (3.36–3.64)	Reference	Reference
Black non-Hispanic	357	1,585,735	2.25 (2.03–2.50)	0.64 (0.58–0.72)	0.49 (0.43–0.56)
Hispanic	1,613	3,974,224	4.06 (3.87–4.26)	1.16 (1.09–1.24)	0.83 (0.77–0.89)
Asian or Pacific Islander	113	513,795	2.20 (1.83–2.64)	0.63 (0.52–0.76)	0.98 (0.80–1.19)
Native American	111	202,628	5.48 (4.55–6.60)	1.57 (1.29–1.89)	1.00 (0.82–1.23)
Other	24	43,835	5.47 (3.67–8.17)	1.57 (1.05–2.34)	0.50 (0.22–1.11)
Fetal number					
Singleton	4,120	12,838,653	3.21 (3.11–3.31)	Reference	Reference
Multiple	68	395,061	1.72 (1.36–2.18)	0.54 (0.42–0.68)	0.77 (0.60–0.98)
Sex of the newborn					
Male	2,377	6,770,524	3.51 (3.37–3.65)	Reference	Reference
Female	2,296	6,463,228	3.55 (3.41–3.70)	1.01 (0.96–1.07)	1.01 (0.95–1.08)

CI, confidence interval.

*States include Arizona, Arkansas, California, Colorado, Georgia, Iowa, Kentucky, New Mexico, New York, Oklahoma, North Carolina, Rhode Island, Texas, Utah, and Washington. 1995 does not include Arkansas, Colorado, Kentucky, North Carolina, New Mexico, Texas, Utah, Washington; 1996 does not include Arkansas, Colorado, Kentucky, North Carolina, New Mexico, Utah, Washington; 1997 does not include Arkansas, Kentucky, North Carolina, New Mexico, Washington; and 1998 does not include Arkansas, North Carolina, and Washington. Data for California and Georgia are for selected counties only.

†Frequencies may not add to total because of missing data.

‡Gastroschisis cases per 10,000 live births.

§Adjusted for all other variables listed in the Table and state of residence.