



**ARIZONA GASTROSCHISIS REPORT
1986-1996**

EPIDEMIOLOGIC REPORT



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GASTROSCHISIS IN ARIZONA, 1986-1996

Executive Summary

This report describes the incidence rate of gastroschisis in Arizona. Gastroschisis is a severe, congenital, abdominal wall defect. Because of recent concern that Arizona may be experiencing increasing rates, we sought to determine the incidence rates of gastroschisis for Arizona and compare them to the national rate. We also considered the practicality of conducting a case-control study of gastroschisis in Arizona. Data for this report is obtained from the Arizona Birth Defects Monitoring Program for the years 1986 through 1996.

Arizona's statewide gastroschisis rate for 1986-1996 is 3.3 cases per 10,000 live births. This overall rate is slightly higher than the national rate of 2 cases per 10,000 live births. We find that a statistically significant increase in cases has occurred between the time periods 1986-1990 and 1991-1996. At this time, we do not recommend a case-control study due to the inherent lack of statistical power to discover causative factors, given the relatively low number of new cases each year above the baseline rate.

We recommend continued monitoring of gastroschisis rates in Arizona, comparison of Arizona's rates with other states' rates, and studies of possible causative factors at a broader (multi-state) level.

Gastroschisis in Arizona, 1986-1996

Background and Purpose of this Report

This report is produced in response to medical community concerns of an elevated number of newborn infants with gastroschisis. These concerns first surfaced in 1995 when doctors and a nurse working in two major referral hospitals in Phoenix believed they were treating an increasing number of gastroschisis cases at their facilities.¹ This issue was brought to the attention of the Arizona Birth Defects Monitoring Program. Upon reviewing the preliminary findings of the local physicians, the Program hired an epidemiologist to determine whether the incidence rate among state residents had increased, and then determine whether a study of gastroschisis would be warranted.

In this report we document Arizona's gastroschisis rate, and determine whether the incidence rate has changed between 1986 and 1996.

What is Gastroschisis?

Gastroschisis is a life-threatening congenital, abdominal wall defect in which the intestines, excluding the umbilical cord, protrude through an opening in the abdomen. Gastroschisis is usually not associated with other birth defects, and 85% of affected infants survive.²

Gastroschisis is believed to occur 5 to 8 weeks after conception, and the current hypothesis regarding the pathogenesis is an early disruption of the right omphalomesenteric artery.^{3,4} Most cases are diagnosed prenatally, and affected newborns require surgical repair of the defect soon after delivery.

Little is known about its etiology. In the United States about two out of every ten-thousand births is affected by gastroschisis. Reports from several countries have documented an increase in the incidence of cases over the past three decades.^{5,6} There are two possible explanations for this increase. First, birth defects such as gastroschisis may be ascertained more accurately by central registries. Second, there may be a new environmental factor. The highest rate of the defect is found in infants of mothers under 20 years of age. However, a biological explanation of the inverse relationship between maternal age and gastroschisis has not been discovered. Recent case-control studies of gastroschisis have evaluated prenatal medication and environmental exposures. For medication exposures, first trimester use of aspirin, ibuprofen, pseudoephedrine, and phenylpropanolamine were each found to significantly elevate the risk for having a baby with gastroschisis.⁷ In addition, early maternal exposure to x-rays and/or organic solvents raised risk levels. Also, use of alcohol, cocaine, marijuana, and smoking were associated with increased risk of gastroschisis.⁷

Data Source and Procedures

The Arizona Birth Defects Monitoring Program (ABDMP) has been in existence since 1986. ABDMP

is a statewide, active surveillance system in which trained abstractors travel to all state birthing hospitals and genetic centers to extract birth defects information from medical records. At the beginning of the study, the ABDMP did not have concurrent data with which to answer the questions asked by the clinicians. By the beginning of the investigation, complete ABDMP data was only available for the years 1986 through 1992, and 1995. To accurately assess gastroschisis in Arizona for the time period of interest, ABDMP conducted a special case-finding investigation. In the interest of timeliness, for the incomplete data years 1993, 1994, and 1996 ABDMP limited its investigation to the seven Arizona hospitals (see Appendix I) which perform surgical repair of gastroschisis. We believe this method of case ascertainment identified all live born cases of gastroschisis born to Arizona residents.

Specifically, ABDMP staff reviewed labor and delivery, neonatal intensive care unit, and autopsy logs, and hospital disease indexes to identify suspect cases of gastroschisis. Then the medical record of all suspect cases were reviewed to confirm the diagnosis. Each case was electronically coded into the registry. ABDMP staff reviewed all abstracts for duplicate information and merged case reports into one final complete record. By state law, ABDMP maintains the confidentiality of all birth defect cases.

Case Definition

Because ICD-9-CM codes do not differentiate between gastroschisis and omphalocele we requested and abstracted all records with any abdominal wall defect. We paid particular attention to correctly distinguish between true cases of gastroschisis and mis-classified cases of omphalocele. We included in our analysis all cases of live birth infants, so that we could compare our rates to national rates. Additionally, we did search for and abstract all fetal death cases (but these cases were included in the analysis). Appendix II. shows fetal death cases by year of occurrence.

ABDMP uses the following criteria for inclusion in the Arizona Registry:

- 1.) Mother's place of residence at the time of birth must be in Arizona. (However, births to residents of Mexico, even if they occur in Arizona, are excluded from the ABDMP registry).
- 2.) Baby's defect must be diagnosed within the first year of life.
- 3.) Stillborn infants are included if they are at least 20 weeks gestational age and have a reportable defect.

Analysis of Data

Our purpose of data analysis is to determine if Arizona has experienced a significant increase over time of babies born with gastroschisis, and if the state defect rate is higher than the U.S. incidence rate. Additional goals are to develop a demographic profile of mothers who may be at risk for having a gastroschisis-affected pregnancy. The development of a demographic profile will help medical providers counsel higher risk patients on prenatal exposure risks.

Two approaches were taken to measure for an increase over time in gastroschisis incidence. First, we grouped data into two time periods, 1986-1990 and 1991-1996 and conducted a proportions test.

Second, we calculated a chi square trend (Mantel extension) test. The Mantel extension tests whether the odds in successive groups increase or decrease compared to the baseline. Baseline data for our trend was 1986 cases. Additionally, we calculated defect rates and 95% Poisson confidence intervals for the years 1986 through 1996.

Findings

We counted 264 cases of gastroschisis that occurred in Arizona between 1986 and 1996. Of these, 247 were live born babies and 17 were fetal deaths. Because most national incidence reports are based upon live births, our analysis focuses on the 247 live born Arizona cases of gastroschisis. The overall rate for this eleven year period is 3.3 cases per 10,000 live births. This rate is slightly higher than the national incidence rate of 2 cases per 10,000 live births.

Table 1. Arizona Gastroschisis Rates Per 10,000 Live Births 1986-1996

| Year | Count | All Live Births | Rate | 95% C.I. |
|-------|-------|-----------------|------|----------|
| 1986 | 16 | 60,822 | 2.6 | 1.5-4.3 |
| 1987 | 17 | 63,320 | 2.7 | 1.6-4.3 |
| 1988 | 19 | 65,544 | 2.9 | 1.7-4.5 |
| 1989 | 17 | 67,128 | 2.5 | 1.5-4.1 |
| 1990 | 18 | 68,814 | 2.6 | 1.5-4.1 |
| 1991 | 32 | 68,040 | 4.7 | 3.2-6.6 |
| 1992 | 24 | 68,675 | 3.5 | 2.2-5.2 |
| 1993 | 14 | 69,037 | 2.0 | 1.1-3.4 |
| 1994 | 26 | 70,896 | 3.7 | 2.4-5.4 |
| 1995 | 27 | 72,386 | 3.7 | 2.5-5.4 |
| 1996 | 37 | 75,094 | 4.9 | 3.5-6.8 |
| Total | 247 | 749,756 | 3.3 | 2.9-3.7 |

Using a proportions test, we find a statistically significant increase ($p=.0099$) in the number of gastroschisis cases between the time frames 1986-1990 and 1991-1996. The rate for 1986-1990 is 2.7 cases per 10,000 live births, while for 1991-1996 the rate is 3.8. Results of our chi square for trend (Mantel extension) showed a statistically significant linear increase ($p=.0123$) in cases over the eleven year time period (1986 to 1996).

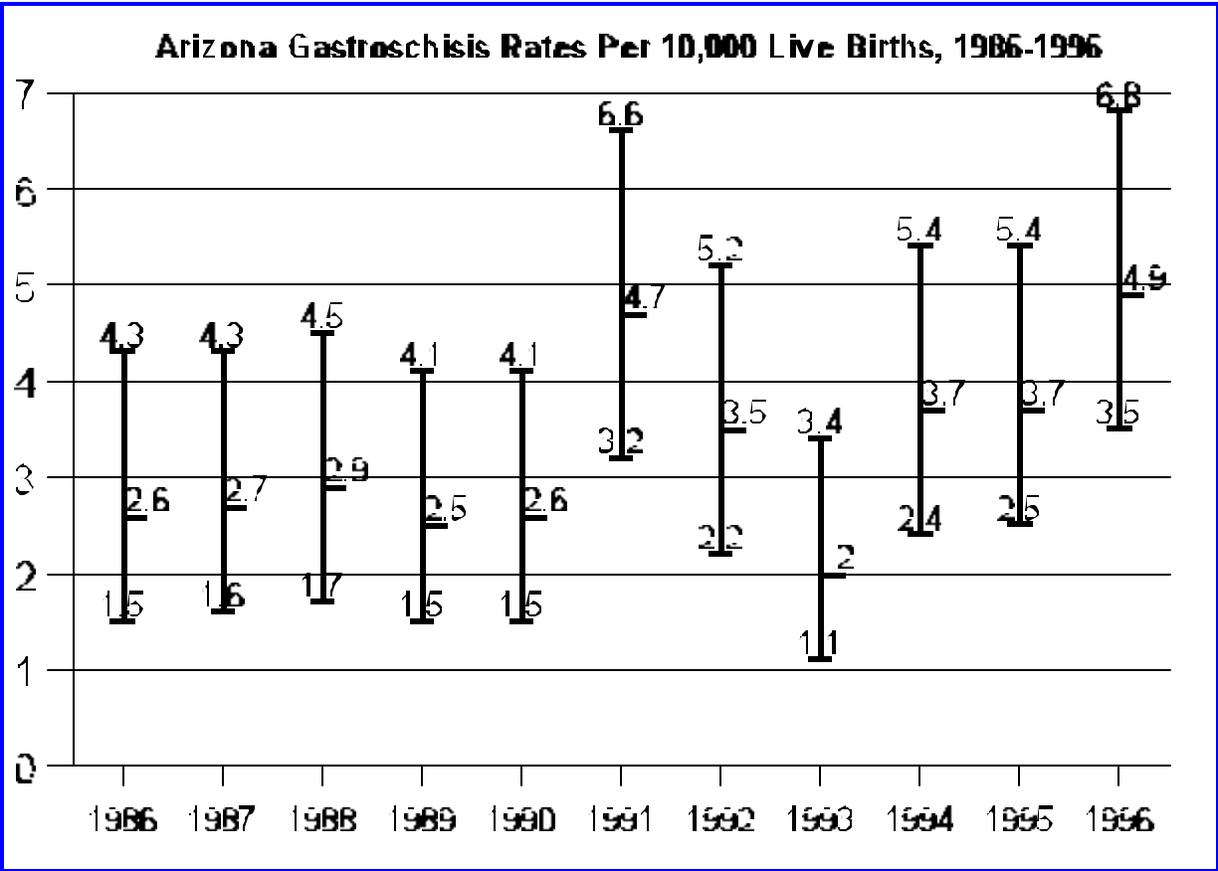


Figure 1. Gastroschisis Rates and 95% Poisson Confidence Intervals Per 10,000 Live Births

There was little difference by sex of the affected babies: slightly more than half (50.6%) were female. Maternal race was predominately White, non-Hispanic (56.3%); 34.0% of mothers were Hispanic. The average age of mothers was 22 years of age, and the range for maternal age was from 14 to 41 years of age. Our data show a disproportionately large number of births to teenage mothers (see Table 4). Overall, 28.3% or 70 cases were born to teenage mothers. Statewide, women 19 years of age and under account for about 15% of Arizona's births.⁸ Nationally, mothers under 20 years of age make up about 13% of all live births.⁹ The proportion of live births attributed to Arizona's teenage mothers has grown slightly almost every year from 1986 to 1996. Lastly, we examined the case mother's county of residence and compared this with Arizona's live birth percentages by county. We found no difference by geographic region.

Table 2. Arizona Gastroschisis Cases by Sex of Child, Live Births 1986-1996

| Sex | Count | Percentage |
|--------|-------|------------|
| Male | 122 | 49.4 |
| Female | 125 | 50.6 |
| Total | 247 | 100.0 |

Table 3. Arizona Gastroschisis Cases by Maternal Race, Live Births 1986-1996*

| Race | Count | Percentage | Percentage of Arizona Births* |
|------------------------|--------------|-------------------|--------------------------------------|
| White, non-Hispanic | 139 | 56.3 | 51.3 |
| Hispanic | 84 | 34.0 | 36.5 |
| Black | 10 | 4.0 | 3.1 |
| Native American Indian | 12 | 4.8 | 7.1 |
| Other/Unknown | 2 | .8 | 2.0 |
| Total | 247 | 100.0 | 100.0 |

*Arizona Live Birth Percentages by Mother's Race/Ethnicity for 1996.

Table 4. Arizona Gastroschisis Cases by Maternal Age, Live Births 1986-1996

| Maternal Age | Count | Percentage | Percentage of Arizona Births* |
|---------------------|--------------|-------------------|--------------------------------------|
| 19 and Younger | 67 | 28.0 | 14.6 |
| 20 - 24 | 114 | 47.7 | 29.0 |
| 25 - 29 | 39 | 16.3 | 28.7 |
| 30-34 | 16 | 6.7 | 19.2 |
| 35 and Older | 3 | 1.3 | 8.5 |
| Total | 239 | 100.0 | 100 |

*Arizona Live Birth Percentages by Maternal Age Group for 1986-1996.

Table 5. Arizona Gastroschisis Cases by Maternal Race and Age, Live Births 1986-1996

| Race/Age | <20 | 20-24 | 25-29 | 30-34 | 35> | Total |
|---------------------|---------------|--------------|--------------|--------------|---------------|--------------|
| White, non-Hispanic | 37 | 60 | 28 | 12 | 2 | 139 |
| Hispanic | 26 | 44 | 9 | 4 | 1 | 84 |
| Black | 1 | 7 | 2 | 0 | 0 | 10 |
| Native American | 6 | 6 | 0 | 0 | 0 | 12 |
| Other/Unknown | 0 | 1 | 0 | 1 | 0 | 2 |
| Total | 70 | 118 | 39 | 17 | 3 | 247 |

Table 6. AZ Gastroschisis Cases by County of Mother’s Residence, Live Births 1986-1996

| County | Count | Percentage of Gastroschisis | Percentage of Arizona Births* |
|---------------|--------------|------------------------------------|--------------------------------------|
| Apache | 2 | .8 | 1.7 |
| Cochise | 4 | 1.6 | 2.3 |
| Coconino | 4 | 1.6 | 2.5 |
| Gila | 1 | .4 | .9 |
| Graham | 2 | .8 | .6 |
| Greenlee | 0 | 0 | .2 |
| La Paz | 0 | 0 | .2 |
| Maricopa | 141 | 57.1 | 62.0 |
| Mohave | 13 | 5.3 | 2.4 |
| Navajo | 3 | 1.2 | 2.3 |
| Pima | 51 | 20.6 | 15.0 |
| Pinal | 8 | 3.2 | 2.8 |
| Santa Cruz | 1 | .4 | 1.1 |
| Yavapai | 6 | 2.4 | 2.1 |
| Yuma | 11 | 4.4 | 3.9 |
| Total | 247 | 100.0 | 100.0 |

*Arizona Live Birth Percentages by Mother’s County of Residence for 1996.

Discussion

This special investigation conducted by the ABDMP shows that Arizona’s gastroschisis rate is slightly higher than the national incidence rate. This may be explained, in part, by Arizona’s higher than average proportion of live births to women under 20 years of age. Another factor influencing Arizona’s rate may be substance abuse. According to the National Institute on Drug Abuse, half of all women who use illicit drugs are in the childbearing age group of 15-44. In addition, the highest percent of illicit drug use in the U.S. is in the region that includes Arizona and 12 other Western states.¹⁰

The major strength of this investigation is its use of timely and complete data for the study years 1986 through 1996. Additionally, multiple sources were used to ascertain cases, so we believe that all, or nearly all live birth cases have been identified.

This investigation also has some limitations. For the sake of timeliness, data for the years 1993, 1994, and 1996 were only reviewed at the seven Arizona hospitals who do surgical repairs of gastroschisis. Also, nine charts not locatable in hospitals were resolved by reviewing the surgeon’s records. There is the possibility that as ABDMP staff complete their statewide surveillance additional cases could be identified. Additionally, 6 suspect patient medical records could not be located at two facilities in

Phoenix (1 case from 1993, 2 cases from 1994, 1 case from 1995, and 2 cases from 1996).

Conclusion

In summary, we confirm the clinicians' observations that Arizona has experienced a statistically significant rise in the rate of gastroschisis cases. An increase is noted between the time periods 1986-1990 and 1991-1996. While this increase is statistically significant, we do not think this magnitude of the elevation is sufficient at this time to warrant a local case-control study. The number of cases that constitute the increase above the baseline rate is too small to allow further investigation that would have any statistical power to detect a cause.

The Centers for Disease Control and Prevention (CDC) currently is sponsoring case-control studies of birth defects, including gastroschisis, in various states around the country. We will await the results of those studies to see how Arizona's rate and demographic profile compare to that of other states, and whether those studies identify additional risk factors for gastroschisis before we consider an Arizona-specific study.

Appendix I

These hospitals were chosen because they provide surgical repair of gastroschisis in Arizona. For all years except 1993, 1994 and 1996 the case ascertainment was from hospitals across the entire state.

1. Desert Samaritan, Mesa.
2. Good Samaritan Regional Medical Center, Phoenix.
3. Phoenix Children's Hospital.
4. St. Joseph's Medical Center, Phoenix.
5. Maricopa Medical Center, Phoenix.
6. Tucson Medical Center.
7. University Medical Center, Tucson.

Appendix II

Note: These counts were not used in the calculation of the rate for live births.

Arizona Gastroschisis Cases, Fetal Deaths 1986-1996

| Year | Count |
|-------|-------|
| 1986 | 3 |
| 1987 | 0 |
| 1988 | 0 |
| 1989 | 2 |
| 1990 | 3 |
| 1991 | 4 |
| 1992 | 3 |
| 1993 | 1 |
| 1994 | 0 |
| 1995 | 0 |
| 1996 | 1 |
| Total | 17 |

*Fetal death - Death prior to the complete expulsion or extraction from its mother of a product of conception that may have reached at least 20 weeks of gestation. The death is indicated by the fact that after such expulsion or extraction the fetus does not breath or show any evidence of life, such as beating of the heart, pulsation of the umbilical cord, or a definite movement of voluntary muscles. If the gestational period is unknown or uncertain, a fetal death certificate is filed if the fetus weighs 500 grams or more.

References

1. California Birth Defects Monitoring Program. Birth Defects Definitions Report, 1997.
2. Hartwig, N.G., C. Vermeij-Keers, H.E. de Vries, m. Kagie, and H. Kragt. Limb-body wall malformation complex: an embryologic etiology? *Human Pathology*., 1989;20:1071-1077.
3. Hoyme, H.E., M.C. Jones, and K.L. Jones. Gastroschisis: abdominal wall disruption secondary to early gestational interruption of the omphalomesenteric artery. *Semin. Perinatology*, 1983;7:294-298.
4. Lindham, S. Omphalocele and gastroschisis in Sweden 1965-1976. *Acta. Paediatr. Scand.*, 1981;70:55-60.
5. Hemminki, K., I. Saloniemi, P. Kyyronen, and M. Kekomaki. Gastroschisis and omphalocele in Finland in the 1970s: prevalence at birth and its correlates. *Journal of Epidemiology and Community Health*, 1982,36:289-293.
6. Torfs, C.P., E.A. Katz, T.F. Bateson, P.K. Lam, and C.J.R. Curry. Maternal medications and environmental exposures as risk factors for gastroschisis. *Teratology*, 1996;54:84-92.
7. Personal communication in 1995 between Tim Flood, M.D. with Ray Jennett, M.D. and Therese Flood, R.N.
8. Mrela, C.K.. Arizona Health Status and Vital Statistics. Office of Health Planning, Evaluation and Statistics. Arizona Department of Health, 1986-1996.
9. National Center for Health Statistics. Monthly Vital Statistics Report, 1997;46:13.
10. Beatrice, R.A.(Editor). Substance abuse and mental health statistics source book. Office of Applied Studies, Substance Abuse and Mental Health Services Administration, 1995:65.