# Mortality among Infants with Congenital Malformations, New York State, 1983 to 1988

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## SYNOPSIS

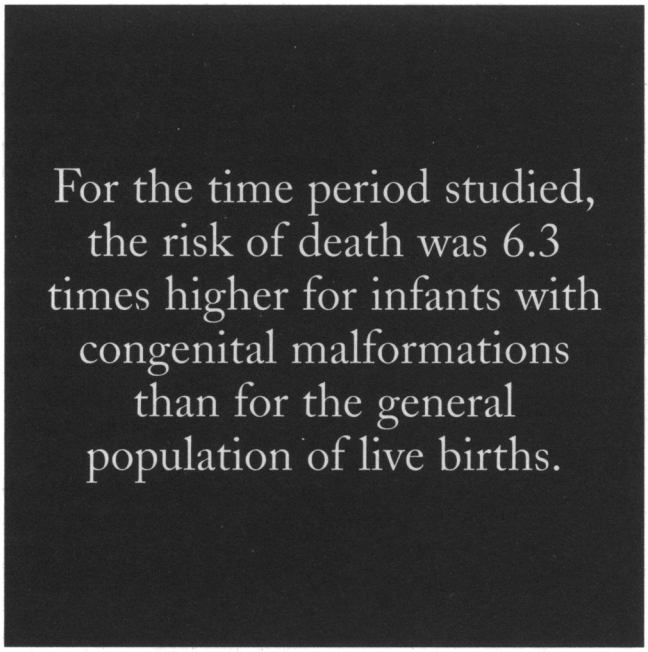
**Objective.** The authors examined first-year mortality and risk factors for mortality among infants with major congenital malformations.
**Methods.** Infants with major congenital malformations born from 1983 to 1988 were identified from a statewide population-based congenital malformations registry. Variables analyzed included year of birth, birth weight, gestational age, infant sex, number of malformations, number of organ systems involved, level of care of the birth hospital, maternal age, maternal education, and maternal ethnicity.
**Results.** Infants with major malformations had a risk of death 6.3 times higher than the general population of live births. The risk declined from 6.5 in 1983 to 5.9 in 1988. Birth weight and number of malformations were the strongest risk factors. The likelihood of survival was similar for white and black infants.
**Conclusions.** Being born with a malformation outweighs most of the other risks for infant mortality. Children with congenital malformations had higher cause-specific mortality for all causes except injury.

Congenital malformations are a leading cause of infant death.[1] The development of birth defects registries in the last 25 years has provided a way to track trends in the occurrence of malformations. In addition, registries can be used for health planning, for needs assessment, and for follow-up studies of the long-term effects of birth defects.[2] While there have been a large number of studies examining infant mortality in general, including risk factors, and the contribution of congenital malformations to infant mortality, far less information is available about the mortality rates of infants with congenital malformations.

The mortality rates of children with congenital malformations is frequently determined from vital records[3,4] or, for specific malformations, from hospital case series.[5,6] However, these sources may be biased in their ascertainment and thus may not accurately reflect the experience of the population. Vital records data are limited by lack of completeness and accuracy in the reporting of birth defects on birth and death certificates.[7-9] A recent study of prune belly using the population-based New York State Congenital Malformations Registry (CMR) for case ascertainment found a higher mortality rate than had previous studies using hospital cases series.[10] Unless all infants were born in-house, a

hospital cases series would probably miss those infants who were born at other institutions and were considered unlikely to survive and thus not transferred for treatment. This would result in an underestimation of mortality.

The available information indicates that while infant mortality due to congenital malformations has fallen since 1960, the overall percentage of infant deaths due to congenital malformations has increased.[3] Studies of cause-specific infant mortality indicate that the decline in mortality is not as great for infants with malformations as for the population as a whole. Berry et al. found a 31% decline in infant mortality due to congenital anomalies from 1960 to 1980 while the infant mortality due to all causes declined 54% in the same time period.[3]




In a national study using vital records data, the black:white ratio for infant mortality due to all causes was about 2:1 in 1960 and 1980.[11] This ratio was unchanged in 1992, according to NCHS data.[1] However, studies have found white and black infants to have similar mortality rates due to congenital malformations.[1,12,13,14]

Very few studies have used data from a birth defects registry to look at mortality. Lynberg et al.,[14] using data from the Metropolitan Atlanta Congenital Defects Program, found that the risk of dying was 6.4 times higher for infants with birth defects than for all live births. The highest mortality was among infants with respiratory tract anomalies, central nervous system anomalies, and autosomal defects.

The present study was undertaken to examine the mortality experience of infants with congenital malformations, ascertained from a statewide population-based congenital malformations registry, and the risk factors for first-year mortality among these infants.

## Methods

The New York State Department of Health's Congenital Malformation Registry (CMR) is a population-based registry that collects information on all children who are born or reside in the state and are diagnosed before the age of two years with a major congenital malformation, including structural, functional, and biochemical abnormalities. Hospitals and physicians are required by state law to report to the CMR. In actuality, most reporting is done by hospitals, but physicians are contacted for further information when a reported diagnosis is unclear or needs to be confirmed. Hospitals are provided with a list of major malformations to be reported to the CMR. Reporting of minor malformations is not required unless they are associated with a major malformation because the ascertainment diagnosis of minor malformations is highly variable and unreliable. The division between major and minor is far from perfect. No standard lists or definitions exist. We used several sources, including the practices of other registries, to develop our list of major malformations. (The list is available from the authors on request.)

Children reported to the CMR are routinely matched to their birth certificates to verify maternal residence and to obtain demographic and birth-related information and birth certificate numbers. Birth certificate matching is carried out by a computer program that compares several variables listed on the birth certificate to data on children reported to the CMR who were born in that year. The variables used in matching include child's last name, date of birth, mother's maiden name, mother's last name, and father's last name. Possible matches are reviewed by CMR staff, and a decision is made as to whether there is a match. Unmatched cases are checked further to see if items have been correctly keyed and all possible aliases have been identified. Over 95% of CMR cases are matched to birth certificates. To determine mortality status, we used a matched birth-death infant mortality file maintained by the New York State Department of Health. These files are created by matching death certificates of children to their birth certificates. Matching is done for children up to one year of age who die in the state. We determined the mortality status of infants reported to the CMR by matching these cases to the birth-death file by birth certificate number. The underlying cause on the death certificate was used to determine cause of death. These were then categorized into eight groups: congenital malformations; causes related to low birth weight and immaturity; causes related to other perinatal and pregnancy conditions; infectious diseases; systemic causes, which includes conditions such as neoplasms; external causes, such as deaths due to injuries; Sudden Infant Death Syndrome; and ill-defined causes, that is, nonspecific causes such as cardiac arrest with no underlying reason given.

We analyzed data on infants who were born in the years 1983 to 1988 to New York State residents, who were diag-

nosed with a malformation before one year of age, and for whom the CMR report could be matched to the birth certificate. We calculated the total number of malformations for each infant. Malformations were categorized into one of 12 organ systems, and the number of systems involved for each infant was determined. The 12 systems are defined as: central nervous, eye, cardiovascular, ear, genitourinary, integument, respiratory, musculoskeletal, oral clefts, digestive, chromosomal, and "other."

Variables included in the analysis were year of birth, birth weight, length of gestation, sex of infant, number of malformations, number of organ systems, place of residence (New York City/New York State outside New York City), level of care of the birth hospital, maternal age, maternal ethnicity, and maternal education.

Birth weights less than 500 g or greater than 7,000 g were considered invalid and recoded as missing. Lengths of gestation less than 16 weeks or more than 45 weeks were also recoded as missing. Maternal ethnicity was classified as black, white, or other. Maternal education was classified as less than a high school education, a high school education (12 years), or more than a high school education.

All hospitals in New York State providing maternal and newborn care are required to participate in the state's perinatal care regionalization system. Within each region some hospitals are designated as Regional Perinatal Care Centers and provide consultation and coordination of perinatal care for the area. Other hospitals receive designations based on the level of care they offer—intensive or intermediate. The remaining hospitals are categorized as providers of regular care.

Infant mortality was calculated overall and for each variable. Relative risks and 95% confidence intervals were calculated to compare different levels of the variables. Logistic regression using Statistical Analysis System's Logistic Regression Procedure (SAS, PROC LOGIST) was performed to determine the effects of each variable on first-year survival while controlling for the other variables.

## Results

For the birth years 1983 to 1988, 61,517 infants were reported to the CMR as having major malformations. We excluded 1029 infants from our analysis because of missing birth certificate numbers. Twenty additional infants were excluded as probable mismatches as the dates of birth and death were inconsistent. This left a total of 60,468 infants, of whom 4138 (68.4 per thousand) died before one year of age. The mortality rate before age one of children reported to the CMR decreased each year for the first four years, from a high of 73.9 per thousand infants in 1983 to a low of 61.1 in 1987, and then increased to 63.9 in 1988 (Table 1). The infant mortality rate for all live births in the state varied from a high of 11.5 per thousand in 1983 to a low of 10.6 in 1986. For 1987 and 1988 the figure increased slightly to 10.7. Overall, for the time period studied, the risk of death was 6.27 times higher for infants with congenital malformations than for the general population of live births. The risk declined somewhat from 6.43 in 1983 to 5.9 in 1988.

Mortality was highest for infants born with respiratory malformations, followed by those with chromosomal defects and central nervous system anomalies.

Congenital malformations were listed as the cause of death for 64% of children with major malformations (Table 2). The next leading cause of death was a group of factors related to low birth weight and immaturity. Children with congenital malformations had higher cause-specific mortality in all of the groups except for "external" causes, for which mortality was the same for those with and without congenital malformations.

An examination of mortality by organ system (Table 3) indicates that mortality was highest for infants born with respiratory malformations, followed by those with chromosomal defects and central nervous system anomalies. Mortality was lowest for those with musculoskeletal malformations.

Mortality for selected maternal and infant characteristics is presented in Table 4. The highest unadjusted mortality was in the extremes of maternal age: infants born to women under age 20 and over age 39. Infants born to mothers with more than a high school education had better unadjusted survival rate than the other education groups. The unadjusted mortality rate was almost three times

**Table 1. First-year mortality in children with congenital malformations and in all live births, New York State, 1983–1988**

| | Deaths per 1000 infants | |
|---|---|---|
| Year | Live births with congenital malformations | All live births |
| 1983 | 73.9 | 11.5 |
| 1984 | 71.1 | 10.9 |
| 1985 | 70.0 | 10.7 |
| 1986 | 70.0 | 10.6 |
| 1987 | 61.1 | 10.7 |
| 1988 | 63.9 | 10.7 |
| Total | 68.4 | 10.9 |

**Table 2. Causes of death in the first year for children with major malformations and for all live births, New York State, 1983–1988**

| Cause of death grouping | Percent of all deaths | | Deaths per 1000 | |
|---|---|---|---|---|
| | Major malformations | All live births | Major malformations | All live births |
| Congenital malformations | 64.0 | 20.1 | 45.1 | 2.5 |
| Low birth weight/respiratory distress syndrome | 12.0 | 33.4 | 8.6 | 4.1 |
| Other perinatal and pregnancy-related causes | 7.8 | 20.9 | 5.5 | 2.6 |
| Infectious diseases | 4.6 | 6.3 | 3.2 | 0.8 |
| Systemic causes | 7.5 | 9.4 | 5.3 | 0.6 |
| External causes | 0.5 | 2.2 | 0.3 | 0.3 |
| Sudden infant death syndrome | 2.0 | 9.4 | 1.4 | 1.2 |
| Nonspecific causes | 1.3 | 2.8 | 0.9 | 0.4 |

higher among children born to black mothers than among those born to white mothers. New York City residence was also associated with higher mortality. While female infants had slightly higher mortality than male infants, the difference was not statistically significant. Decreasing birth weight was associated with increasing mortality, as were increasing numbers of malformations or systems involved. Unadjusted mortality rates were similar among the different levels of hospitals, with a slightly better chance of survival for infants born at regular or Level I hospitals.

The results of the logistic regression (Table 5) indicate similar survival rates for whites and blacks after adjusting for the other factors. Infants born to women ages 40 and over still had higher mortality than other groups, but this difference was no longer statistically significant. Infants of women with more than a high school education continued to have better survival than those born to mothers in the other education groups. Mortality continued to be higher in infants with lower birth weight, a greater number of malformations, and multiple organ system involvement. Mortality was very similar among the different levels of care provided by hospitals. Mortality risk did not differ by sex or by residence.

**Table 3. First-year mortality by organ system in children with congenital malformations, New York State, 1983–1988**

| Organ system | Number of children | Deaths | Deaths per 1000 infants |
|---|---|---|---|
| Cardiovascular | 15,795 | 1991 | 126.1 |
| Central nervous system | 4,056 | 828 | 204.1 |
| Chromosomal | 2,248 | 490 | 218.0 |
| Cleft | 2,060 | 212 | 102.9 |
| Digestive | ,640 | 450 | 67.8 |
| Ear | 295 | 29 | 98.3 |
| Eye | 1,168 | 143 | 122.4 |
| Genitourinary | 9,085 | 675 | 74.3 |
| Integument | 137 | 8 | 58.4 |
| Musculoskeletal | 20,179 | 964 | 47.8 |
| Respiratory | 2,620 | 719 | 274.4 |
| Other | 5,844 | 563 | 96.3 |

## Discussion

This paper has presented absolute and relative risks for mortality among infants with major congenital malformations using data from a statewide birth defects registry. Overall, for the time period, the risk of death for children with major malformations was 6.27 times higher than for the general population of live births. This is similar to the 6.4-fold elevation found by Lynberg et al.[14] Our findings of the highest mortality rates in children with respiratory, chromosomal, and central nervous system anomalies and an overall downward trend over time in mortality for infants with malformations were also noted by Lynberg et al.[14]

The major risk factors for mortality in infants with malformations found in both the unadjusted and adjusted analyses were related to birth weight, gestational age, number of malformations, which organ system was involved, and the number of organ systems involved. The traditional demographic factors associated with general infant mortality, (maternal age, maternal education, maternal ethnicity, and infant's sex) did not show strong relationships with mortality in infants with congenital malformations. Birth weight and gestational age, which are strongly associated with general infant mortality, did show strong associations with mortality of infants with birth defects.

The risk among infants born to women with more than a high school education was somewhat lower than in other educational groups. Educational status is traditionally used as a proxy for socioeconomic status, which has been associated with variation in the occurrence of certain birth defects, most notably the neural tube defects.[15] The association of educational status with infant mortality could also reflect a difference in access to health care services.

Infants of older mothers had a higher risk of death, although this was not statistically significant in the multivariate analysis. This might reflect the higher risk of chromosomal anomalies in older women[16] and thus a tendency for more lethal anomalies. Because of the number of women in this age group was small, it is unclear whether this finding represents a real difference reflecting the higher risk for chromosome anomalies[16]—and a corresponding risk for lethal anomalies—among older women.

**Table 4. Infant mortality for children with major malformations by selected maternal and infant characteristics, New York State, 1983 to 1988**

| | Number | Deaths | Deaths per 1000 infants | Relative Risk | 95% Confidence Interval |
|---|---|---|---|---|---|
| Mother's age | | | | | |
| Less than 20 | 6,342 | 485 | 76.5 | 1.16[b] | 1.05–1.28 |
| 20 to 24 | 15,204 | 1,051 | 69.1 | 1.05 | 0.97–1.14 |
| 25 to 29[a] | 19,126 | 1,259 | 65.8 | — | — |
| 30 to 34 | 13,728 | 906 | 66.0 | 1.00 | 0.92–1.09 |
| 35 to 39 | 5,084 | 349 | 68.6 | 1.04 | 0.93–1.17 |
| 40 or more | 960 | 84 | 87.5 | 1.33[b] | 1.08–1.64 |
| Mother's education | | | | | |
| Less than high school | 12,304 | 932 | 75.7 | 1.09 | 1.01–1.18 |
| High school[a] | 24,037 | 1,663 | 69.2 | — | — |
| More than high school | 22,196 | 1,262 | 56.9 | 0.82[b] | 0.77– 0.88 |
| Missing | 1,931 | | | | |
| Mother's ethnicity | | | | | |
| White[a] | 45,449 | 2,910 | 64.0 | — | — |
| Black | 13,014 | 1,063 | 81.7 | 1.28[b] | 1.19–1.36 |
| Other | 1,546 | 107 | 69.2 | 1.08 | 0.90–1.30 |
| Missing | 459 | | | | |
| Residence | | | | | |
| New York City | 24,657 | 1,793 | 72.7 | 1.11[b] | 1.05–1.18 |
| Upstate New York[a] | 35,811 | 2,345 | 65.5 | — | — |
| Sex | | | | | |
| Female | 26,763 | 1,886 | 70.5 | 1.05 | 0.99–1.12 |
| Male[a] | 33,705 | 2,252 | 66.8 | — | — |
| Birth weight | | | | | |
| Less than 1,500 grams | 3,911 | 955 | 244.2 | 6.36[b] | 5.93–6.83 |
| 1,500 to 2,499 grams | 7,329 | 1,129 | 154.0 | 4.01[b] | 3.74–4.30 |
| 2,500 or more grams[a] | 48,836 | 1,874 | 38.4 | — | — |
| Missing | 392 | | | | |
| Length of gestation | | | | | |
| Less than 37 weeks | 11,268 | 1,717 | 152.4 | 3.26[b] | 3.07–3.46 |
| 37 or more weeks[a] | 47,003 | 2,197 | 46.7 | — | — |
| Missing | 2,197 | | | | |
| Number of malformations | | | | | |
| 1[a] | 48,167 | 1,873 | 38.9 | — | — |
| 2 | 7,606 | 948 | 124.6 | 3.21[b] | 2.98–3.45 |
| 3 | 2,349 | 496 | 211.2 | 5.43[b] | 4.96–5.94 |
| 4 or more | 2,346 | 821 | 350.0 | 9.00[b] | 8.38–9.66 |
| Number of systems | | | | | |
| 1[a] | 53,615 | 2,467 | 46.0 | — | — |
| 2 | 5,026 | 949 | 188.8 | 4.10[b] | 3.83–4.40 |
| 3 or more | 1,827 | 722 | 395.2 | 8.59[b] | 8.02–9.20 |
| Birth hospital | | | | | |
| Regular[a] | 25,255 | 1,588 | 62.9 | — | — |
| Intermediate care center | 5,749 | 411 | 71.5 | 1.14[b] | 1.02–1.26 |
| Intensive care center | 12,514 | 827 | 66.0 | 1.05 | 0.97–1.14 |
| Regional care center | 16,945 | 1,312 | 77.4 | 1.23[b] | 1.15–1.32 |

[a]Reference category.

[b]95% confidence interval does not include 1.

**Table 5. Infant mortality for children with major malformations, New York State, 1983–1988: adjusted odds ratios for selected maternal and infant characteristics**

| | Adjusted Odds Ratio | 95% Confidence Interval |
|---|---|---|
| Mother's age | | |
| Less than 20 | 0.96 | 0.84–1.10 |
| 20 to 24 | 1.01 | 0.92–1.11 |
| 25 to 29[a] | – | – |
| 30 to 34 | 0.96 | 0.87–1.06 |
| 35 to 39 | 0.91 | 0.79–1.05 |
| 40 or more | 1.12 | 0.85–1.48 |
| Mother's education | | |
| Less than high school | 0.92 | 0.84–1.00 |
| High school[a] | – | – |
| More than high school | 0.89[b] | 0.81–0.98 |
| Mother's ethnicity | | |
| White[a] | – | – |
| Black | 0.96 | 0.87–1.05 |
| Other | 1.05 | 0.83–1.32 |
| Residence | | |
| New York City | 1.05 | 0.97–1.15 |
| Upstate New York[a] | – | – |
| Sex | | |
| Female | 0.98 | 0.92–1.06 |
| Male[a] | – | – |
| Birth weight | | |
| Less than 1,500 grams | 6.07[b] | 5.35–6.88 |
| 1,500 to 2,499 grams | 3.07[b] | 2.78–3.38 |
| 2,500 or more grams[a] | – | – |
| Length of gestation | | |
| Less than 37 weeks | 1.28[b] | 1.16–1.41 |
| 37 or more weeks[a] | – | – |
| Number of malformations | | |
| 1[a] | – | – |
| 2 or more | 3.49[b] | 3.14–3.88 |
| Number of systems | | |
| 1[a] | – | – |
| 2 or more | 1.92[b] | 1.72–2.15 |
| Birth hospital | | |
| Regular[a] | – | – |
| Intermediate care center | 1.06 | 0.93–1.21 |
| Intensive care center | 1.05 | 0.95–1.17 |
| Regional care center | 1.04 | 0.95–1.15 |

[a]Reference category.

[b]95% confidence interval does not include 1.

The lack of apparent effect of the level of care provided by the birth hospital probably does not mean that a high level of care is of no importance for these infants. The improved survival over time is likely to be related to advances in medical care. Many infants with congenital malformations who survive the immediate newborn period are transferred to higher level institutions. It may be that some infants with malformations who are born at smaller institutions and transferred after birth will have survival rates similar to infants born at higher level institutions, in contrast to preterm infants, who appear to do better when the mother is transferred before the baby's birth.[17] However, this study was not designed to and can not examine this question in depth. Any effect would vary greatly by specific malformation, which should be considered in future studies.

Intuitively, our findings are not surprising. The fact that an infant has a malformation seems, in general, to outweigh most of the other usual risks for infant mortality. What is more important is the type and number of malformations. It should also be kept in mind that infants with congenital malformations had higher cause-specific mortality for all causes of death except those defined as external and therefore are at risk from a wide range of causes.

There are major limitations to this study. The CMR relies on case reports, obtained primarily from hospitals, to ascertain cases. While some cases may not have been reported to the registry, ascertainment of infants with malformations is certainly far more complete than is possible through birth certificates. As a check on ascertainment, the CMR routinely compares the prevalences of malformations to prevalences found in other registries that use staff to actively ascertain cases. CMR prevalences compare favorably (Unpublished data, C. Druschel, 1994). It also reassuring that our findings were similar to those of a study using data from the Metropolitan Atlanta Congenital Defects Program,[14] which does actively ascertain cases.

Another limitation is that birth defects include a large number of heterogeneous conditions. Individual malformations will have very different patterns of risk and will vary in their potential for correction. The musculoskeletal group, the group with the lowest mortality, includes infants with congenital hip dislocation, who should have low mortality, and infants with deformations resulting from the oligohydramnios sequence, who have very high mortality. The respiratory group, with the highest mortality, includes conditions such as laryngeal web that are correctable as well as agenesis of the trachea, which is not. Many of the deaths in this category were of infants having hypoplastic lungs. This condition frequently results from compression secondary to another malformation such as congenital diaphragmatic hernia or renal agenesis. Future studies will examine the mortality experience of infants with specific malformations.[18]

Prevention strategies have been categorized as primary (avoiding the malformation's occurrence), secondary (prenatal detection and medical treatment or termination), and tertiary (surgical correction).[19] Czeizel et al. estimated that by using all three prevention approaches about 50% of congenital anomalies could be prevented.[19] Primary prevention of congenital malformations is becoming more of a reality. Progress toward the elimination of congenital rubella through immunization[20,21] as well as progress in counseling and treating women with diabetes mellitus and phenylke-

tonuria before pregnancy are examples.[22–25] The recent development in prevention of neural tube defects by an adequate intake of folic acid is very exciting.[26,27] Preliminary studies have hinted that reductions may be possible in other defects as well and provide hope that other means of prevention will be found.[28–31]

But as the etiology and prevention of most congenital malformations remains unknown,[32] we must still rely on tertiary approaches to reduce the mortality of children born with malformations. Progress had been made in improving outcomes for many of these infants. A population-based birth defects registry provides the opportunity to track the mortality experience of infants with malformations. Meanwhile, families should have access to services, including good medical care and follow-up, support services, and genetic counseling to improve the outcome for the whole family.

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