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Young Maternal Age and Congenital Malformations: A Population-Based Study

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ABSTRACT

This study examined the prevalence of congenital malformations across the maternal age spectrum and identified specific malformation types that contributed to the overall prevalence among mothers under the age of 20 years. Data were derived from the California Birth Defects Monitoring Program for 1983 through 1988 live births. The distribution of prevalences of all nonchromosomal malformations was U-shaped across maternal age. Furthermore, several specific malformation types, representing nearly every organ system, were elevated among the infants of women under 20 years of age in comparison with those of women 25 to 29 years old. (*Am J Public Health.* 1995;85:710–713)

Introduction

Since the mid-1980s, pregnancy and birth rates among American teenagers have been increasing, with an estimated 11% of all women between the ages of 15 and 19 becoming pregnant, half of whom go on to deliver a live-born infant.[1,2] Few studies, however, have investigated the risk for congenital malformations among the offspring of teen mothers. This issue deserves attention, particularly given that low birthweight and infant mortality are outcomes for which infants of teen mothers are at high risk.[3] Congenital malformations are associated with low birthweight and are the leading cause of infant mortality in the United States.[4] Furthermore, factors suspected of playing a role in the etiology of some malformations such as poor diet, illicit drug use, and smoking may be more common during the pregnancies of young mothers than during those of older mothers.

The few investigations of congenital malformations among offspring of very young mothers have described a U-shaped curve for overall malformation rates across maternal ages.[5,6] These studies have been based on very small sample sizes, have relied on vital statistics malformation data, and have not described specific malformation types contributing to the pattern.

Using population-based registry data, we examined the prevalence of congenital malformations across the maternal age spectrum and attempted to identify specific types contributing to the overall prevalence of malformations among the youngest women.

Methods

Infants with congenital malformations were identified by the California Birth Defects Monitoring Program, a population-based congenital malformation registry with active ascertainment from multiple sources. Nearly all structural anomalies diagnosed before an infant's first birthday, including those diagnosed prenatally, are included in the registry.[7] Overall ascertainment has been estimated as 97% complete.[8] However, registry reportability procedures result in variable ascertainment for malformations

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TABLE 1—Demographic Characteristics of Malformed Infants and Total Live Births: California, 1983 through 1988

	Malformed Live Births, %	Reference Population, %
Maternal age, y		
≤15	0.7	0.7
16	1.3	1.1
17	2.0	1.9
18	2.8	2.7
19	3.9	3.7
20–24	25.9	26.1
25–29	30.6	32.0
30–34	21.9	22.2
35–39	9.1	8.3
≥40	1.9	1.3
Child sex		
Male	59.8	51.2
Female	40.2	48.8
Maternal race/ethnicity		
White non-Hispanic	55.8	54.5
White Hispanic	24.3	24.0
Black	7.8	7.4
Asian	5.7	7.5
Other	6.4	6.5
Parity		
Firstborn	43.7	41.5
Second born	29.7	32.0
Third born	14.9	15.5
≥fourth born	11.3	10.7
Unknown	0.3	0.3
Plurality		
Singleton	96.3	97.9
Multiple	3.4	2.1
Unknown	0.3	. . .
Maternal birthplace		
California	47.6	46.7
Mexico	12.2	11.9
US (excluding California)	25.5	24.9
Elsewhere	14.2	16.4
Unknown	0.5	0.1

Note. For the malformed live birth group, n = 29 848; for the reference population, n = 1 028 255.

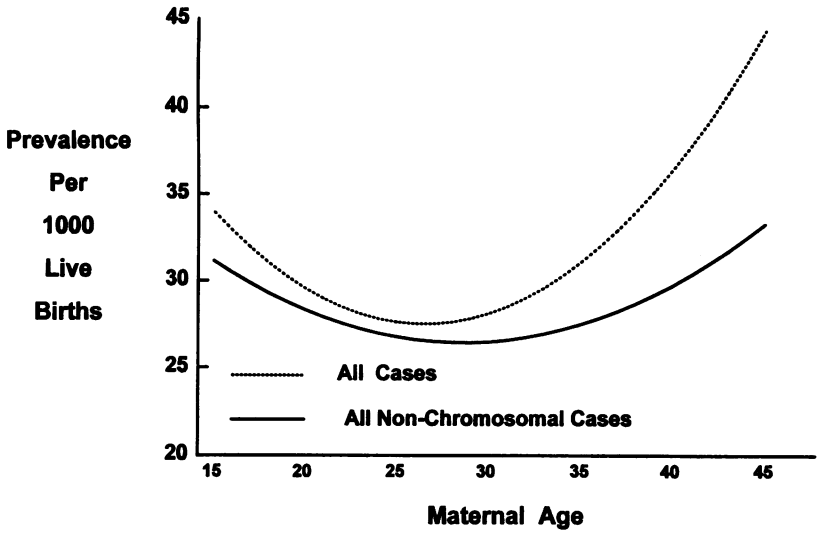


FIGURE 1—Prevalence of congenital malformations across maternal age: California, 1983 through 1988.

that are not medically significant, such as skin tags. Furthermore, ascertainment of elective terminations is conditional on diagnoses made in hospitals or genetic centers and is thus incomplete.

In this study, case patients were malformed children who were born alive in 1983 through 1988 and whose mothers resided, at the time of delivery, in one of 55 California counties. The population at risk included all children born alive in 1983 through 1988 to residents of these same counties. Maternal age and other demographic variables for all infants were derived from California birth certificate files.

The prevalence of all malformations combined was calculated for each maternal age between 15 and 45 years. As a means of smoothing the prevalence curve, weighted least squares regression with S-Plus[9] was performed to model malformation prevalence across the age distribution. Age was included in the regression model in single years. Because of the U-shaped curve observed for prevalence of malformations across maternal ages, age was modeled with both a linear term and a quadratic term (model: $y = a + b^*\text{age} + c^*\text{age}^2$). Age-specific prevalences and weighted least squares regression curves were computed both including and excluding infants with chromosomal anomalies, conditions known to be associated with advanced maternal age.[10]

Age-specific prevalences for nonchromosomal cases were also examined by sex, maternal race/ethnicity (White non-Hispanic, White Hispanic, Black, Asian, other), parity (0, 1, 2, or 3+ previous births), plurality (singleton, multiple), and maternal place of birth (California, other US state, Mexico, other).

As a means of identifying specific malformations that contributed to the increased prevalence among the youngest women, the prevalence among women less than 20 years of age for each four-digit malformation code of the *International Classification of Diseases* (ICD) (codes 740.0 to 759.9) was compared with the prevalence among women between 25 and 29 years old. This age group was chosen as a reference because it had the lowest overall prevalence and contained the largest number of women. These four-digit codes probably contain etiologically dissimilar phenotypes; nevertheless, they are more specific anatomically than the three-digit codes that describe malformations at the organ system level only. Infants were represented in each diagnostic group for which they had a diagnosis. Relative risks, defined as the ratio of the prevalences for the two age groups (less than 20 years and 25 to 29 years), and corresponding 95% confidence intervals were calculated for each diagnosis.

Results

Among 1 028 255 live births, 29 848 malformed infants were identified, a prevalence of 29.1 per 1000 live births. Six percent (n = 1793) of case infants had a chromosomal anomaly. Approximately 11% of the case infants and 10% of the overall birth population had mothers under the age of 20 years (Table 1). In comparison with the birth population, case infants were more likely to be male (59.8% vs 51.2%) and less likely to be

TABLE 2—Prevalence of Nonchromosomal Congenital Malformations, by Maternal Age and Race/Ethnicity: California, 1983 through 1988

Maternal Age, y	White Non-Hispanic	White Hispanic	Black	Asian	Other
<20					
No. of cases	1286	1087	422	88	169
Prevalence per 1000 live births	31.2	27.8	29.1	23.9	32.3
95% confidence interval	29.6, 32.9	26.2, 29.4	26.4, 31.9	19.3, 29.5	27.8, 37.6
20–24					
No. of cases	3798	2229	705	254	416
Prevalence per 1000 live births	28.3	27.5	28.5	20.6	26.4
95% confidence interval	27.4, 29.2	26.4, 28.6	26.4, 30.6	18.1, 23.2	23.9, 29.0
25–29					
No. of cases	5151	1874	643	514	538
Prevalence per 1000 live births	27.1	26.5	29.9	19.9	25.4
95% confidence interval	26.4, 27.9	25.3, 27.7	27.6, 32.2	18.3, 21.7	23.3, 27.6
30–34					
No. of cases	3791	1051	349	457	422
Prevalence per 1000 live births	27.5	27.1	30.2	19.2	26.0
95% confidence interval	26.7, 28.4	25.5, 28.7	27.2, 33.5	17.5, 21.0	23.6, 28.5
35–39					
No. of cases	1477	428	116	181	183
Prevalence per 100 live births	29.3	29.8	31.5	18.3	26.8
95% confidence interval	27.8, 30.8	27.1, 32.7	26.1, 37.7	15.7, 21.1	23.1, 30.9
≥40					
No. of cases	226	102	14	57	27
Prevalence per 1000 live births	30.9	36.2	29.8	30.0	23.7
95% confidence interval	27.1, 35.1	29.6, 43.8	16.4, 49.5	22.8, 38.7	15.7, 34.4

Asian (5.7% vs 7.5%); however, the two populations were similar in terms of other demographic factors (Table 1).

Figure 1 depicts prevalence curves across maternal age for all malformations, including and excluding chromosomal cases. For all cases, prevalence across the age distribution was J shaped, with women 25 to 29 years of age having the lowest prevalence, women less than 20 years old having an intermediate prevalence, and women more than 39 years old having the highest prevalence. After exclusion of infants with a chromosomal anomaly, the prevalence of malformations dropped substantially for women more than 40 years of age but only marginally for other age groups, resulting in a U-shaped curve.

Among nonchromosomal cases, a similar U-shaped prevalence curve was seen for females and males, firstborn and second-born infants, singletons, and women born in California and Mexico (data not shown). For multiple births, the prevalence of malformations was highest among the youngest mothers (72.9 per 1000 in women under 17 years of age) and declined with increasing maternal age (43.2 per 1000 in women more than 39 years old). Although the U-shaped pattern was not seen for the Black race/ethnic group, it was observed for the White non-Hispanic, White Hispanic, and Asian groups (Table 2).

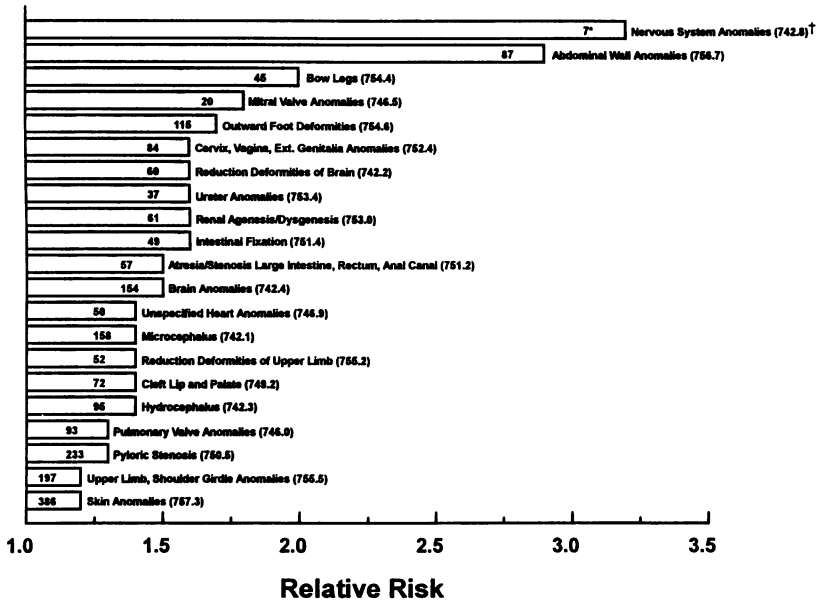
Figure 2 shows the specific four-digit diagnostic categories, listed in order of descending relative risk, that were more prevalent among mothers under 20 years old than among mothers 25 to 29 years old. For presentation purposes, only diagnoses that had a relative risk greater than 1.0 and a 95% confidence interval excluding 1.0 are shown. The 21 diagnoses reflect nearly every organ system. While defects of the central nervous system and upper limbs and deformations were frequently represented, major heart defects were nearly absent. After removal of case infants with any one of the 5 most frequent ICD four-digit conditions (anomalies of skin, upper limb and shoulder girdle, brain, pyloric stenosis, and microcephalus), the shape of the prevalence curve persisted, suggesting that the increase in prevalence for all malformations among women less than 20 years of age is not completely explained by the most common conditions.

Discussion

Our findings among more than 1 000 000 births suggest that women at the extremes of the age distribution have an increased risk for congenital malformations relative to women in the middle of the distribution. Furthermore, the risk for nonchromosomal defects among women less than 20 years of age is comparable to that among the oldest group of mothers (those more than 40 years old). Several malformation types, representing nearly every organ system, were found to be elevated among the offspring of women under 20 years old in comparison with the infants of 25- to 29-year-old women. Some types, such as gastroschisis and pyloric stenosis, have been reported previously.[11–17] While a U-shaped pattern of prevalence across maternal age was observed for Whites and Asians, no age differences were apparent among Blacks. With regard to our results, issues of ascertainment and classification need further discussion.

Our ascertainment of malformations depends on the completeness and accuracy of medical records. The observed increase in malformation prevalence among women less than 20 years of age may be partially explained by diagnostic bias. Because of the known association between young maternal age and poor pregnancy outcome,[3] offspring of teenagers may come under heavier scrutiny by medical practitioners, potentially leading to differential ascertainment of selected conditions with respect to maternal age. We were unable to directly assess the potential for such bias; however, the fact that numerous types of malformations, many of which were severe, were identified among younger mothers indirectly argues against such a bias being the primary explanation for our findings.

Analyses were restricted to live births, and variability by age in the use of



Note. A list of specific diagnoses included in each category is available from the authors. * = number of cases among mothers younger than 20 years old; † = ICD 4-digit code.

FIGURE 2—*International Classification of Diseases* (ICD) 4-digit congenital malformation diagnoses with increased prevalence among mothers younger than 20 years of age: California, 1983 through 1988.

prenatal screening and subsequent elective termination of malformed conceptuses could have affected our findings. In comparison with 25- to 29-year-old women, approximately 6% fewer women younger than 20 begin prenatal care by the end of the second trimester[18] and may have less opportunity to terminate an affected fetus. Assuming that the malformation prevalence among these women is identical to that among young women delivering live-born infants, this 6% difference does not explain the increased prevalence among younger women. It is also possible that lower fetal loss and stillbirth rates for malformed conceptuses among younger women could explain our results. While we are not aware of any data on age-specific rates of spontaneous abortion among malformed conceptuses, the frequency of chromosomally normal spontaneous abortion is the same for both age groups,[19] as is the proportion of malformed conceptuses that are stillborn (unpublished registry data).

The identification of specific malformation types that contributed to the overall prevalence of malformations among women less than 20 years of age may have been influenced by the categorization of mother's age. The use of different age cut points may result in different malformation types being identified as elevated among "young mothers." However, our findings for nervous system defects, cleft lip and palate, anomalies of female genitalia, deformations, upper limb defects, anomalies of the abdominal wall, and anomalies of the skin held regardless of the young age cut point used.

The difference in the maternal age relation observed across race/ethnicity is intriguing. The lack of an increased risk for the youngest Black women may be due to differences across race/ethnic groups in (1) age-dependent malformation prevalences, (2) ascertainment of malformations, or (3) the representatives of the age reference group.

It remains to be clarified whether the increased risk of malformations among young mothers is due to behavioral or developmental factors and when, relative to conception, these factors may be etiologically important. Such factors warrant investigation, given the high rates of pregnancy among teenagers in the United States. □

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