

Risk for Neural Tube Defect–Affected Pregnancies among Women of Mexican Descent and White Women in California

ABSTRACT

Objectives. This study investigated a previously reported 50% or more increased risk for neural tube defect–affected pregnancies among Latina women compared with White women.

Methods. Data were derived from a population-based case–control study of fetuses and live-born infants with neural tube defects in a 1989-through-1991 California birth cohort. Interviews were conducted with mothers of 538 (88% of eligible) infants/fetuses with neural tube defects and mothers of 539 (88%) nonmalformed control infants.

Results. The risk for a neural tube defect–affected pregnancy was approximately twice as high among women of Mexican descent than among White women (odds ratio = 1.9, 95% confidence interval [CI] = 1.5, 2.8). The odds ratio for Mexico-born Mexican women compared with White women was 2.4 (95% CI = 1.7, 3.2), whereas the risk for US-born women of Mexican and other racial/ethnic descent was not substantially higher than that for Whites. The higher risk among Mexico-born Mexican women was not attributable to differences in numerous studied parental characteristics and exposures.

Conclusions. Given that nearly 20% of all California births are to Mexico-born Mexican women, the increased risks observed are relevant to the population burden of neural tube defects. (*Am J Public Health.* 1997;87:1467–1471)

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Introduction

Few identified factors, other than lack of maternal intake of vitamins containing folic acid, account for much of the population burden of neural tube defects (spina bifida and anencephaly). Considerable ethnic and geographic differences in prevalence have been reported for these common congenital anomalies, which contribute substantially to childhood morbidity and infant and fetal mortality.¹ The prevalence of neural tube defects, for example, varies from approximately 0.7 per 1000 births in many areas of the United States to 3.5 per 1000 in Mexico.^{1–4} Studying such ethnic and geographic differences has been a fertile area in epidemiologic research for several disease entities, particularly if a change in risk is observed following migration.⁵ Studies have shown that the risks of Latina women in the United States for delivering offspring with neural tube defects are 1.5 to 3 times as high as the risk for non-Latina Whites.^{3,6–11} Among these studies, only two also explored the possible association with mother's nativity, that is, whether foreign-born Latinas were at greater risk than US-born Latinas of delivering affected offspring.^{9,11} Further, earlier studies that showed an increased risk among Latinos did not have information on potential risk factors, beyond what is routinely collected in birth and fetal death registration, with which to explore possible risk factors that might contribute to the increased risk of neural tube defects.

We focused our analyses on women of Mexican descent because most Latinos living in California are of Mexican descent. Using data from a large California population-based case–control study, we investigated whether Mexico-born

Mexican women were at greater risk for having neural tube defect–affected pregnancies than were US-born women of Mexican descent or White women. We also investigated potential risk factors to explore why Latinas are at increased risk, compared with Whites, of neural tube defect–affected pregnancies.

Methods

For this population-based case–control study, details of which have been reported previously,¹² infants or fetuses with a neural tube defect were ascertained by reviewing medical records, including prenatal diagnostic records, at all hospitals and genetic clinics for infants/fetuses who were delivered in selected California counties and whose mother gave her residence as California. Singleton fetuses and live-born infants diagnosed with a neural tube defect among the cohort of 708 129 births from June 1989 through May 1991 and fetuses diagnosed prenatally with a neural tube defect and electively terminated from February 1989 through January 1991 were eligible. Ascertained were 653 case infants/fetuses. Control infants were randomly selected from each area hospital in proportion to the hospital's estimated contribution to the total population of infants born alive in a given month from June 1989 through May 1991. Ascertained were 644 singleton infants who were born alive without a

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TABLE 1—Risks for Offspring with Neural Tube Defects among Maternal Racial/Ethnic Groups: California, 1989 through 1991

Maternal Racial/Ethnic Group	Case Subjects (n = 538), No.	Control Subjects (n = 539), No.	Odds Ratio	95% Confidence Interval
White	215	271	Reference	. . .
Mexican descent	230	155	1.9	1.4, 2.4
Mexico-born	172	91	2.4	1.7, 3.2
US-born	58	64	1.1	0.8, 1.7
Other Latina	36	42	1.1	0.7, 1.7
Other	57	71	1.0	0.7, 1.5

reportable congenital anomaly¹³ and whose mothers were California residents.

In-person interviews were conducted with mothers in English (74%) or Spanish (26%). Women who spoke only a language other than English or Spanish (29 case mothers and 32 control mothers), as well as 12 women who had had a previous neural tube defect-affected pregnancy, were excluded. Interviews were completed with mothers of 538 (87.8%) case infants/fetuses (217 with anencephaly, 296 with spina bifida, and 25 with other neural tube defects) and with mothers of 539 (88.2%) control infants, an average of 4.9 months for case subjects and 4.6 months for control subjects after the actual or estimated date of term delivery.

The average 2-hour interview elicited information on maternal medical, reproductive, and family history; employment; hobbies; vitamin intake (including food supplements); activities associated with various lifestyle factors; and some factors concerning the baby's father. A woman was shown a list of 22 racial/ethnic groups and asked which group best described her racial or ethnic background. Women were also asked if they were of Spanish or Hispanic descent. With respect to nativity and length of residence in the United States, women were asked, "Where were you born (country, city, and state)?" and "In what year did you first move to the United States?" Women were asked the corresponding questions about the baby's father. Information about daily intake of dietary folate during the 3 months before conception was obtained for 1007 women (916 revealed suitable data on the basis of error checks built into the analytic software) who completed a self-administered food-frequency questionnaire.¹⁴ Also included as part of that questionnaire were questions regarding social support before pregnancy: "How many close friends did you have?" and

"How many relatives did you have that you felt close to?"

To investigate the potential influence of neighborhood socioeconomic conditions, maternal residences from 3 months before conception through the end of the first trimester for 480 (78.3% of eligible) case mothers and 499 (81.7%) control mothers were linked to characteristics of the 1990 US census block groups. Block groups, assumed to represent neighborhoods, were characterized as follows: "Less" neighborhood education was assigned to block groups where 45% or more of the residents 18 years or older did not graduate high school or its equivalent. "High" neighborhood poverty level was assigned to block groups where 20% or more of the noninstitutionalized residents lived below the federal poverty level (\$12 674 for a family of four in 1989). "Operator/laborer" neighborhoods were block groups where 20% or more of the employed residents 16 years or older worked in operator/laborer occupations. Neighborhood "crowding" was assigned to block groups where 20% or more of the occupied housing units had more than one person per room. Analytic cutpoints were defined by changes in neural tube defect risk, although little variability in risks across potential cutpoints was observed.

Odds ratios and their 95% confidence intervals were computed by means of EGRET.¹⁵ Analyses were performed to estimate risk of neural tube defect-affected pregnancies among three groups of women: Mexican, born in Mexico (Mexico-born Mexican); Mexican, born in the United States (US-born Mexican); and White. Analyses were also performed on numerous potential risk factors to determine whether they contributed to the increased risk of neural tube defects observed among Mexico-born Mexican women.

Results

All case mothers, compared with all control mothers, were more likely to be younger than 25 years of age (43% vs 34%), more likely to have a household income less than \$10 000 (25% vs 15%), less likely to have graduated from college (17% vs 28%), and less likely to have consumed alcohol during the first trimester (28% vs 34%). Case mothers were also more likely to be of Mexican descent (odds ratio [OR] = 1.9; 95% confidence interval [CI] = 1.4, 2.4) (Table 1). The risk for having a neural tube defect-affected pregnancy was more than twice as high among Mexico-born Mexican women than among White women (OR = 2.4, 95% CI = 1.7, 3.2) (Table 1). However, for US-born Mexican women or for women in other racial/ethnic groups, including "other" Latinas, risks were not substantially higher than the risk for Whites (Table 1). Approximately 95% of both case and control White mothers were born in the United States. Among Mexico-born Mexican women, case mothers had lived in the United States an average of 1.5 years less than control mothers (mean = 6.6 years for case and 8.1 for control mothers; *t*-test *P* = .06) at time of delivery.

We explored the increased risk of neural tube defects observed for Mexico-born Mexican mothers compared with Whites across strata of selected covariates (Table 2), several of which have been associated with risk of neural tube defects. Except for mothers who were employed as managers, who had less neighborhood education, or who had diabetes, or for fathers who were young (<20 years) or who were not employed in the period 3 months before conception, elevated odds ratios (similar to the overall odds ratio) were observed for most covariate strata, which suggests that variability in selected covariates did not contribute substantially to the increased risk of neural tube defects among Mexico-born Mexican mothers. Adjustment for each of these factors did not substantially change the observed increased risk of neural tube defects. Other maternal factors relating to the time around conception, including gravidity, body mass index, dietary folate intake, recreational drug use, epilepsy, heat stroke or heat exhaustion, use of herbal medications or medicinal teas, pica behaviors, or activities such as furniture stripping, gardening, or painting, also did not substantially contribute to the increased

risk of neural tube defects observed for Mexico-born Mexican mothers (not shown). As determined by an industrial hygienist's exposure-assessment approach, described elsewhere,¹⁶ occupational exposures to the following materials did not explain the increased risk either: colorants, fungicides, herbicides, insecticides, other pesticides, dyes and pigments, plastics, propellants, solvents, household cleaners, and pyrolysis/combustion products. Mexico-born Mexican women were at increased risk for both anencephaly and spina bifida as well as for their phenotypic subcategories.

Simultaneous adjustment for maternal age, education, gravidity, use of vitamin supplements, alcohol use, cigarette smoking, marital status, employment, household income, body mass index, dietary folate intake, and paternal race/ethnicity and education revealed an odds ratio of a neural tube defect-affected pregnancy for Mexican-born women of 2.2 (95% CI = 1.1, 4.3); this suggests little evidence for confounding by these factors (analysis restricted to women whose baby's father was employed in the 3 months before conception because paternal employment appeared to modify the risk of neural tube defects). In contrast, simultaneous adjustment for neighborhood socioeconomic conditions (neighborhood education, poverty, occupational level, and crowding) did reveal evidence for confounding (adjusted OR of a neural tube defect-affected pregnancy for Mexico-born Mexican women of 1.4; 95% CI = 1.0, 2.1).

Consideration of the ethnic backgrounds of both parents (excluding 17 parent pairs in which the mother reported that she and the baby's father were blood relatives) revealed that the increased risk of neural tube defects among Mexico-born Mexican mothers appeared limited to those infants/fetuses whose mothers and fathers were both of Mexican descent (Table 3). Elevated risks of neural tube defects were observed for Mexico-born Mexican fathers irrespective of mothers' ethnicity.

Discussion

These data show that for Mexico-born Mexican mothers and fathers, the risk of having offspring with a neural tube defect is more than twice as high as it is for White mothers and fathers. The increased risk among Mexico-born Mexicans is consistent with earlier reports of higher prevalences of neural tube defects

TABLE 2—Risks (Odds Ratios) for Having a Neural Tube Defect—Affected Pregnancy among Mexico-Born Mexican Women Relative to White Women, by Category of Potential Covariates: California, 1989 through 1991

	Mexico-Born Mexican		Odds Ratio	95% Confidence Interval
	No. Case Subjects	No. Control Subjects		
Overall	172	91	2.4	1.7, 3.2
Maternal age, y				
≤19	32	14	2.0	0.8, 5.0
20–24	58	35	1.8	1.0, 3.3
25–29	44	20	2.6	1.4, 4.8
30–34	26	18	1.9	1.0, 3.8
≥35	12	4	6.0	1.8, 19.8
Paternal age, y				
≤19	7	6	0.6	0.1, 2.8
20–24	51	21	3.0	1.5, 5.9
25–29	55	29	2.7	1.6, 4.8
30–34	29	18	1.9	1.0, 3.6
≥35	28	16	2.3	1.1, 4.8
Maternal education				
<High school	132	68	2.0	1.1, 3.5
High school graduate	33	17	2.3	1.2, 4.3
College graduate	6	5	1.8	0.6, 5.9
Paternal education				
<High school	121	68	1.7	1.0, 3.1
High school graduate	32	12	3.2	1.6, 6.4
College graduate	13	8	2.5	1.0, 6.1
Neighborhood education				
Less	89	41	1.1	0.44, 2.6
More	47	36	1.7	1.1, 2.9
Maternal employment from 3 months before to 3 months after conception				
No	80	37	2.5	1.5, 4.2
Yes	92	54	2.2	1.5, 3.3
Maternal US Census occupation group				
Managerial/professional	2	7	0.4	0.1, 2.5
Technical/sales/clerical	17	8	2.1	0.8, 5.8
Service	31	20	2.5	1.1, 5.6
Farm/fishing/forestry	18	8	6.8	0.5, 199.3
Production/craft/repair	5	1	5.0	0.2, 298.4
Operators/laborers	18	7	5.1	1.1, 26.6
Paternal employment 3 months before conception				
No	11	13	0.5	0.2, 1.7
Yes	158	76	2.7	1.9, 3.7
Paternal US Census occupation group				
Managerial/professional	4	5	1.2	0.3, 5.2
Technical/sales/clerical	10	5	1.7	0.5, 6.4
Service	27	11	3.3	1.2, 9.3
Farm/fishing/forestry	43	30	1.4	0.5, 4.1
Production/craft/repair	15	9	2.4	0.9, 6.7
Operators/laborers	52	16	5.6	2.5, 12.4
Operator/laborer neighborhood				
No	64	51	1.7	1.1, 2.7
Yes	72	26	1.6	0.8, 3.5
Household income				
<\$10 000	68	34	1.4	0.7, 2.8
\$10 000–\$29 999	49	29	2.7	1.5, 4.8
\$30 000–\$49 999	7	5	1.5	0.5, 4.7
≥\$50 000	5	2	4.1	0.8, 16.6
Neighborhood poverty				
Low	54	38	1.9	1.2, 3.1
High	82	39	1.6	0.8, 3.2
Neighborhood crowding				
No	45	32	1.8	1.1, 3.1
Yes	91	45	1.5	0.7, 3.1

(Continued)

TABLE 2—Continued

	Mexico-Born Mexican		Odds Ratio	95% Confidence Interval
	No. Case Subjects	No. Control Subjects		
Marital status				
Married	110	67	2.1	1.5, 3.0
Not married, living with partner	42	14	3.4	1.6, 7.2
Not married, living alone	15	6	4.4	1.3, 15.2
Widowed, divorced, or separated	5	4	1.3	0.3, 6.1
Social support, close friends				
None	48	13	1.9	0.4, 10.5
1–2	77	51	2.1	1.3, 3.4
3–5	20	19	1.3	0.7, 2.6
≥6	7	2	4.3	0.8, 16.4
Social support, close relatives				
None	50	18	3.9	1.1, 12.6
1–2	71	45	1.7	1.0, 2.8
3–5	25	16	2.3	1.2, 4.5
≥6	6	6	1.3	0.4, 3.9
Child sex				
Male	78	43	3.6	2.3, 5.8
Female	88	48	2.2	1.4, 3.4
Periconceptional use of vitamins containing folic acid^a				
None	106	58	1.5	0.9, 2.5
3 months before conception	7	3	2.7	0.7, 9.0
Started use in first trimester	56	28	3.2	1.9, 5.3
Cigarette use, first trimester				
None	152	87	2.1	1.5, 2.9
Any	20	4	6.5	2.3, 19.6
Alcohol use, first trimester				
None	147	73	2.3	1.6, 3.3
Any	25	18	2.0	1.0, 3.8
Maternal diabetes				
No	161	80	2.5	1.8, 3.5
Yes ^b	9	11	1.2	0.3, 4.2
Maternal fever				
No	136	81	2.4	1.7, 3.4
First trimester	32	7	4.0	1.6, 10.0

^aIncludes vitamin supplements and food supplements containing folic acid.

^bIncludes non-insulin-dependent mothers.

among Latinos^{3,6–11} as well as with the approximately fourfold higher prevalence of neural tube defects (relative to California non-Latino White births) in Mexico.⁴ Only two earlier studies investigated whether the risk of neural tube defects was higher among first-generation Latina immigrants than among second-generation or later immigrants.^{9,11} In a study of a Los Angeles cohort of births from 1973 through 1977, mother's birth in Mexico was associated with an increased risk for spina bifida but not for anencephaly.⁹ A more recent, smaller study conducted in Harris County, Texas, did not find a higher risk among Latina mothers born in Mexico than among Latinas born in Texas for either spina bifida or anencephaly.¹¹ Our study indicates that first-generation Latinas are at greatest risk of having neural tube defect-affected pregnancies with spina bifida or anencephaly; it also indicates that first-generation immigrant case mothers had, on average, a shorter length of residency in the United States at time of conception than did first-generation control mothers.

Our study—in addition to having population-based ascertainment and being larger than previous studies—explored extensive interview data for maternal (and paternal) factors, such as diabetes, nutritional intake, socioeconomic status, and maternal occupation, that might account for the increased risk among the Mexico-born Mexican women. We were, however, unable to identify a particular covariable that explained the increased risk of neural tube defects for this group of women. Maternal factors considered likely to contribute to the increased risk, given their postulated role in the occurrence of neural tube defects, were lack of use of vitamin supplements (including food supplements) containing folic acid; diabetes; and occupational exposures, particularly pesticide exposures. For example, we did not find evidence to suggest that a lack of use of vitamins near the time of conception might have contributed to the increased risk; in fact, risk estimates were higher for those women who used supplements. The number of Mexico-born Mexican women who used vitamins around the time of conception was very small, however, and therefore risks among those women could not be adequately investigated.

We did find some evidence (on the basis of adjusted risk estimates) to suggest that socioeconomic conditions associated with where individuals lived (e.g., neighborhood education, poverty, occupational

TABLE 3—Risks (Odds Ratios) for Offspring with Neural Tube Defects among Maternal and Paternal Racial/Ethnic and Nativity Groups: California, 1989 through 1991

Maternal Race/Ethnicity and Nativity	Paternal Race/Ethnicity and Nativity		
	White	US-born Mexican	Mexico-born Mexican
White			
No. cases/controls	169/221	12/17	9/7
Odds ratio	Reference	0.9	1.7
95% CI	...	0.4, 2.0	0.6, 4.6
US-born Mexican			
No. cases/controls	9/16	26/27	16/11
Odds ratio	0.7	1.3	1.9
95% CI	0.3, 1.7	0.7, 2.2	0.9, 4.2
Mexico-born Mexican			
No. cases/controls	3/4	10/5	141/78
Odds ratio	1.0	2.6	2.4
95% CI	0.2, 4.4	0.9, 7.8	1.7, 3.3

Note. This analysis excludes 17 parent pairs in which the mother reported that she and the baby's father were blood relatives. CI = confidence interval.

level, and crowding) may have contributed to the observed increased risks. There will need to be further exploration of how these socioeconomic conditions specifically contribute to the risk of neural tube defects among Mexico-born women.

Our results are not likely to be due to selection bias resulting from variable completeness of case ascertainment or from variable participation among those eligible. It is possible that risk estimates could have been artifactually elevated if case ascertainment was more complete among Mexico-born Mexicans than among Whites, owing, for example, to less complete ascertainment of case infants among White women as a result of their more frequent use of prenatal diagnosis and elective termination procedures. Such differential ascertainment is unlikely, however, given the study's population-based nature and its use of multiple sources for case ascertainment, including those for the identification and enrollment of women who elected to terminate a pregnancy because of a neural tube defect. Further, the participation of eligible case and control mothers in the interview was quite high (approximately 90%), and nonparticipants were similar to study participants in race/ethnicity.

Finding an increased occurrence of neural tube defects among Mexico-born Mexican women is inconsistent with findings associated with other adverse reproductive outcomes, for example, low birthweight.¹⁷ Yet in general, foreign-born Latinas are more socioeconomically disadvantaged than Whites and US-born Latinas, and lower socioeconomic status has been linked with the occurrence of neural tube defects.^{1,18} Nutritional factors have been identified as contributors to the etiology of neural tube defects, and subpopulations of Latinas have been identified as being at increased risk for multiple nutrient deficiencies.^{19,20} However, diet (excluding vitamin supplement use) has been shown to be markedly better

in first-generation Latinas than in second-generation or White non-Latina women.²¹ A possible nutritional explanation for the increased neural tube defect risk in Mexican-born Mexican women requires further investigation.

Given that California births represent one of seven births in the United States and nearly 20% of all births in California are to Mexico-born Mexican women (according to the present study), the increased risks of neural tube defects that we observed are relevant to the population burden of neural tube defects. □

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