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Folic Acid and Prevention of Spina Bifida and Anencephaly

10 Years After the U.S. Public Health Service Recommendation

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Folic Acid and Prevention of Spina Bifida and Anencephaly

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Introduction

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In September 1992, the U.S. Public Health Service (USPHS) recommended that all women capable of becoming pregnant should consume 400 µg of folic acid/day on an ongoing basis to reduce their risk for having a pregnancy affected by spina bifida and anencephaly (i.e., neural tube defects [NTDs]) (*1*). The recommendation was preceded a year earlier by a CDC recommendation for women at high risk (i.e., those women who have had an earlier pregnancy affected by an NTD). The 1991 CDC recommendation stated that women at high risk should plan subsequent pregnancies and consume 4,000 µg/day of folic acid from the time they begin trying to become pregnant through the first trimester of pregnancy to reduce their risk (*2*). The 1992 USPHS recommendation specified that women at high risk should follow the general population recommendation for consumption of 400 µg/day when not trying to become pregnant (*1*).

Both of these recommendations were based on scientific evidence that increased folic acid consumption reduced the risk for having a pregnancy affected by an NTD. In 1983, a nonrandomized but controlled trial that studied multivitamins containing folic acid determined that folic acid might prevent NTDs (*3*). In 1991, the British Medical Research Council (MRC)-sponsored randomized controlled trial indicated that folic acid alone could reduce the risk for NTD-affected pregnancies among women who had had an earlier NTD-affected pregnancy (*4*). In 1992, a randomized controlled trial in Hungary reported the protective effect of folic acid-containing multivitamins against first occurrences of NTDs (*5*). These two controlled and randomized studies, together with consistent results from multiple observational studies, prompted the 1992 USPHS recommendation.

The 1992 USPHS recommendation stated that increased folic acid consumption could be achieved in three ways: by increasing consumption of foods rich in naturally occurring folates, by increasing use of folic acid-containing dietary supplements, and by fortification of a staple foodstuff (e.g., flour). In 1998, a report from the Food and Nutrition Board of the Institute of Medicine (IOM) stated that women of reproductive age should consume 400 µg/day of folic acid from dietary supplements or from fortified foods, in addition to eating a healthy diet containing natural folate compounds (*6*).

Since 1992, efforts have been made to increase daily use of dietary supplements containing 400 µg of folic acid by women of reproductive age. Additionally, in 1998, the Food and Drug Administration began requiring the fortification of enriched cereal grain products with folic acid at the level of 140 µg/100 grams of grain (fortification was optional during March 1996–December 1997). This level of fortification was chosen to assist women of reproductive age in increasing their folic acid consumption by an average of 100 µg of folic acid daily.

This issue of the *MMWR Recommendations and Reports* presents data to assess the impact of efforts to prevent NTDs through increased folic acid consumption. Blood folate levels for U.S. women of reproductive age from the National Health and Nutrition Examination Survey (NHANES) for the combined years of 1999 and 2000 were substantially higher than those determined for the NHANES III samples collected during 1988–1994 (*7*). Because substantial increases have not occurred in the reported use of folic acid-containing dietary supplements during 1995–2002 (*8*), the assumption is that the majority of this rise in blood folate levels is the result of consumption of fortified cereal grain products (e.g., bread and pasta) and from fortified ready-to-eat breakfast cereals. In addition to an increased availability of folic acid derived from fortified flour, a substantial number of ready-to-eat cereals have had increases in their folic acid content (CDC, unpublished data, 2002). Certain subgroups of the population have experienced more limited increases in blood folate levels than has the general population of reproductive-age women. One group of women attending family planning clinics in Georgia had a median serum folate level of 8.9 ng/mL, compared with the NHANES 1999–2000 median of 13.0 ng/mL (*9*). The reasons for this difference are unknown but could include a lower level of folic acid consumption among subgroups of the U.S. population. If so, such subgroups could possibly benefit from

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targeted interventions to promote increased folic acid consumption from breakfast cereals and dietary supplements. In China, an intensive campaign to encourage use of folic acid supplements among women planning to start a pregnancy was highly successful in reducing NTDs among the population (*10*).

NTD rates have declined by approximately 20%–30% since the institution of folic acid-fortified cereal grains (*11–13*). This decrease is expected on the basis of predicted increases in folic acid consumption from fortified cereal grains (100 µg/day) (*14*). In contrast, the decrease in NTD rates is not the 50%–70% decrease predicted by USPHS in 1992 (*1*), if all women of reproductive age were to consume 400 µg of folic acid/day. The decrease is also lower than what could be predicted on the basis of the substantial rise in blood folate levels among U.S. women of reproductive age. Spina bifida rates in North Carolina appear to have decreased less among disadvantaged segments of the population (*12*). Possibly, women who are most at risk for having NTD-affected pregnancies do not consume as much fortified food products; they do not have the same level of access to other sources of folic acid and could benefit from targeted interventions; or they do not absorb as much folic acid as do women who are at lower risk.

In 1995, approximately 52% of reproductive-age women were aware of the term *folic acid*, and this increased to 80% in 2002 (*8*). However, just 20% of women participating in a 2002 March of Dimes survey knew that folic acid could prevent certain birth defects, and the proportion who stated that they took a vitamin supplement containing folic acid daily increased from 25% in 1995 to only 31% in 2002 (*8*). These findings indicate that educational efforts directed at women of reproductive age might have had an impact on knowledge and to a lesser extent on behavior. According to polls taken by multiple groups, including the March of Dimes (*8*), women of reproductive age state that the recommendation of a physician or other health-care provider would positively influence their decision to take folic acid-containing dietary supplements. However, only a minority of women who are currently using a supplement identify their physician as a source of information. A study in Florida (CDC, unpublished data, 2002) reported that approximately 90% of physicians who responded to a survey knew that folic acid can prevent NTDs but that a more limited proportion could identify the recommended daily dose of 400 µg for the general population; furthermore, an even more limited proportion could state the recommended dose of 4,000 µg for women at high risk. This indicates a need for more educational efforts directed at physicians and other health-care providers.

Among women who are at high risk for an NTD-affected pregnancy because they have had an NTD-affected pregnancy or have spina bifida themselves, approximately 33% reported regular use of a supplement, and only 48% indicated that they believed that folic acid is effective in reducing the risk for an NTD (CDC, unpublished data, 2002). A Texas case-control study reports that 56% of women who have had an infant with an NTD recall receiving postpartum advice to use folic acid, compared with 26% of mothers in the control group. Women who received advice were more likely to use supplements regularly than women who did not (41% versus 22%) (*15*).

These reports reflect the encouraging progress made to increase folic acid consumption by women of reproductive age and reduce the proportion of babies born with NTDs. However, more work needs to be done to reach the goal of preventing all NTDs that could be avoided if all women who become pregnant were to follow the 1992 USPHS recommendation. In addition to the work that needs to be done to prevent NTDs, as discussed in the articles in this report, the policies related to folic acid consumption need to be reviewed and evaluated, and more research is required to improve understanding regarding the causes of NTDs. The Food and Drug Administration mandate to fortify flour and other cereal grain products has had a positive impact on the folate status of the U.S. population. Nevertheless, more birth defect prevention could possibly be achieved by a higher level of grain fortification or by fortification of additional types of foods. Physicians and scientists need a better understanding of what proportion of NTD cases that now occur result from inadequate folic acid consumption and what proportion result from causes unrelated to folic acid. Thus, more research is needed to better understand the biological mechanism by which folic acid prevents NTDs and the causes of those cases that are not connected with folic acid consumption.

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Serum Folate Levels Among Women Attending Family Planning Clinics — Georgia, 2000

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Summary

Since 1998, serum folate levels have increased nationally after mandatory fortification of cereal grain products with folic acid. Whether serum folate levels have increased among all women has not been well-studied. Identifying characteristics of women with lower serum folate levels would also be helpful in designing educational campaigns. Data for this report were collected during January 2000–January 2001. During 2000, blood samples were collected from 1,059 women aged 18–45 years who attended six family planning clinics in Georgia and analyzed for serum folate levels. This sample included women aged 18–25 years (60%), black women (41%), and women who had a high school education or less (49%). The median serum folate level (8.9 ng/mL) among this population was lower than the median of women of childbearing age (13.0 ng/mL) who participated in the 1999–2000 National Health and Nutrition Examination Survey (NHANES). In logistic regression analysis, women who were black (odds ratio [OR] = 2.4; 95% confidence interval [CI] = 1.48, 3.96), who smoked (OR = 2.1; 95% CI = 1.26, 3.43), or who used Depo-Provera® contraceptive injection (manufactured by Pharmacia Corporation, Peapack, New Jersey) (OR = 2.3; 95% CI = 1.15, 4.62) were more likely to be ranked in the lowest quartile (≤6.2 ng/mL) of serum folate concentrations when compared with the highest quartile (>12.4 ng/mL). Women who consumed cereal regularly (OR = 0.4; 95% CI = 0.26, 0.62) or folic acid supplements (OR = 0.2; 95% CI = 0.09, 0.30) were the least likely to be in the lowest serum folate quartile. This study indicates that certain women are at greater risk for having lower serum folate levels, including women who are black, smokers, Depo-Provera users, and those less likely to eat cereal regularly or to take folic acid supplements. In Georgia, these data are useful in defining target populations (e.g., black women and smokers) for folic acid education campaigns because public health officials can develop contextually appropriate messages and outreach approaches for targeting women for folic acid interventions. Ongoing surveillance of serum folate status among women can guide future intervention efforts.

Introduction

Neural tube defects (NTDs), which are serious birth defects of the brain and spinal cord, affect approximately 4,000 pregnancies each year in the United States (*1*). Epidemiologic studies demonstrate that folic acid, when taken in adequate amounts periconceptionally, can prevent 50%–70% of NTDs (*2*). During 1992, the U.S. Public Health Service (USPHS) recommended that all women of childbearing age take 400 µg of folic acid to help prevent neural tube defects (*2*). During 1996, as a way to increase consumption of folic acid among women of childbearing age, the Food and Drug Administration mandated that, effective January 1998, synthetic folic acid be added to enriched cereal grain products (*3*). Reports from the 1999 National Health and Nutrition Examination Survey (NHANES) demonstrates that serum folate levels among childbearing age women have increased after fortification. Median serum folate levels increased from 5.2 ng/mL in NHANES III (1991–1994) to 13.0 ng/mL in NHANES 1999–2000 for women aged 15–44 years (*4*). Whether serum folate levels have risen equally among all women is not yet known. Certain women might still be at an increased risk for having a pregnancy affected by an NTD as a result of inadequate folic acid intake.

Serum folate data from subpopulations of women seeking routine clinical services would be helpful in assessing whether inadequacies exist. In addition, identifying characteristics associated with women who have low serum folate levels would help in designing educational interventions targeted at those with greatest need for higher folic acid consumption. In this study, we report serum folate levels of women before their participation in a folic acid intervention evaluation study in Georgia family planning clinics during 2000. Only limited studies postfortification have examined serum folate levels among populations in the United States (*5,6*). This study attempts to identify a group of women at high risk for low folic acid intake.

Methods

Data Collection

Data were collected from a separate study designed to evaluate the effectiveness of a folic acid intervention in family planning clinics in Georgia. During spring 1999, a total of 163 surveys were mailed to county nurses and health directors in Georgia. Of 118 clinics responding to the survey, 63 clinics were interested in participating in the evaluation. Of these 63 clinics, six had the necessary staff, laboratory resources, and patient volume needed for inclusion as a study site. The six family planning clinics participated in the evaluation during a 12-month period that began in January 2000. The folic acid intervention was developed by the Georgia Family Planning Health Program, which provides family planning and health services to approximately 167,000 female clients annually. The majority of the women served by the Georgia Family Planning Program have low-paying jobs or are unemployed (i.e., ≥150% of the federal poverty level), and many are uninsured (*7*). The folic acid evaluation measured consumption of cereal, folic acid supplements, or multivitamins before and after folic acid education during the study period (January 2000–January 2001). Of women aged 18–45 years who visited these clinics, 1,059 (60.2%) participated in the study. Informed consent was obtained in accordance with CDC's Institutional Review Board guidelines. Participants provided venous blood samples and completed a self-administered questionnaire that collected demographic information, health-related habits, knowledge regarding folic acid, and folic acid consumption. Only data obtained from participants' first visits (i.e., preintervention) were used in this analysis. Blood samples were analyzed for serum folate by using the Bio-Rad Quantaphase® II simultaneous folate/vitamin B_{12} radioassay (Bio-Rad Laboratories, Hercules, California) by the same CDC laboratory that analyzed the NHANES samples (*4*). The blood assay results were linked to data from the questionnaire.

Analysis

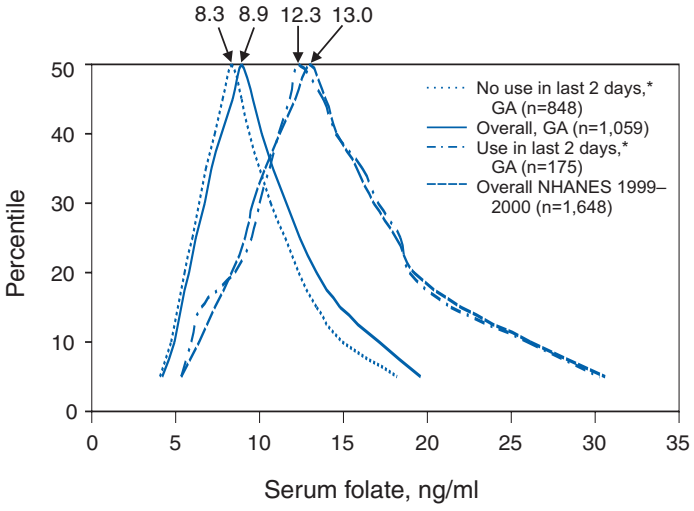
Variables used in the analysis included age, race, educational level, smoking, and folic acid supplement or multivitamin intake within the previous 2 days of the visit, number of servings of breakfast cereal eaten within 2 days of the visit, pregnancy intention, marital status, and contraception method. Folic acid intake within the past 2 days was selected because recent folic acid use substantially affects blood concentration of the vitamin (*8*) and because we believed this to be a more conservative measure of reported use. Only 24 (2%) women reported being of Hispanic, Latino, or Spanish origin, and they were excluded from multivariate analyses because their numbers were too limited to provide reliable or stable estimates. Another 2% of the sample included women who reported being American Indian, Asian, Pacific Islander, or other, and they were excluded from the multivariate analysis also because their numbers were too limited to provide reliable estimates. The remainder of the sample included women who reported being black or white.

The question used to assess folic acid intake was, "In the last 2 days, did you take a folic acid pill or multivitamin?" We used multivariate logistic regression to compare women in the lowest serum folate quartiles (≤6.2 ng/mL) with women in the highest serum folate quartile (>12.4 ng/mL).

Results

The median serum folate level for the 1,059 study participants who attended family planning clinics was 8.9 ng/mL (range: 1.6–164.0 ng/mL) for the overall sample. Women who reported using a folic acid pill or multivitamin during the previous 2 days had a median level of 12.3 ng/mL (range: 3.4–164.0 ng/mL), and women who reported no use during the previous 2 days had a median serum folate level of 8.3 ng/mL (range: 1.6–34.1 ng/mL) (Figure). The serum folate distribution from a nationally representative sample, NHANES 1999–2000, has a median of 13.0 ng/mL, a value that is similar to the median for the women in the Georgia sample who reported either taking a folic acid supplement or a multivitamin during the 2 days preceding the visit (Figure).

FIGURE. Serum folate levels from women aged 18–45 years attending family planning clinics in Georgia (GA) in 2000, compared with folate levels of women aged 15–44 years in the National Health and Nutrition Examination Surveys (NHANES) in 1999–2000



* Reported folic acid supplement or multivitamin use in the previous two days.

Women in this sample were primarily aged 18–25 years (60%); 41% were black; 42% used oral contraceptives; 33% were smokers; and the majority were not married (Table 1). In the adjusted logistic regression model, women who had serum folate levels in the lowest quartile were more likely to be black, use Depo-Provera® contraceptive injection (manufactured by Pharmacia Corporation, Peapack, New Jersey), smoke, and report not eating breakfast cereal or using a folic acid pill or multivitamin during the 2 days preceding the visit (Table 2).

Discussion

When compared with serum folate levels in a nationally representative sample (NHANES 1999–2000), the median in this sample of women attending Georgia family planning clinics during 2000 was substantially lower (*4*). These findings are also inconsistent with findings of improved folate status among other subsets of the U.S. population postfortification (*5,6*). The population of Georgia women in this study differs from the 1999 NHANES population (representative of the U.S. population) by certain characteristics that could explain the lower serum folate levels. For example, the women who participated in the Georgia family planning clinics were more likely to be young, black, and unmarried compared with other U.S. women aged 18–45 years. Possibly, these women differ in their nutritional practices, which could result in differences in serum folate levels when compared with a national sample.

TABLE 1. Sociodemographic and behavioral characteristics of women attending family planning clinics — Georgia, 2000

Variable	Number	%
Race/ethnicity		
White	586	56.4
Hispanic	24	2.3
Black	429	41.3
Age (yrs)		
18–25	629	59.7
26–35	296	28.1
36–45	129	12.2
Education		
Eighth grade or less	16	1.5
Some high school	137	13.0
High school graduate or GED	361	34.2
Some college or trade school	437	41.4
College graduate	105	9.9
Marital status		
Married	236	22.3
Not married	820	77.7
Birth control method		
Birth control pill	421	42.4
Depo-Provera®*	237	23.8
Barrier/withdraw	120	12.1
Other	63	6.3
None	153	14.4
Smoking status		
Any cigarettes smoked/day	348	33.2
None	701	66.8
Folic acid use		
Used during previous 2 days	175	17.1
None	848	82.9
Cereal consumption		
Any bowls eaten during previous 2 days	412	39.2
None eaten	639	60.8
Total†	**1,059**	—

* Contraceptive injection (manufactured by Pharmacia Corporation, Peapack, New Jersey).
† Numbers might not total 1,059 because of missing data.

During 2000, approximately 34% of women aged 18–45 years reported taking folic acid daily (*9*). In this sample, only 17% reported taking folic acid during the previous 2 days. The 2000 Gallup poll sample included 21% women aged 18–24 years and only 11% black women (*9*). In contrast, this sample had a greater proportion of women who were aged 18–25 years (60%) and black (56%). In addition, only 6% of family planning clinic patients reported, "planning to get pregnant in the next few months or next year." Folic acid consumption might be viewed by these women as a behavior associated with pregnancy planning. Because the majority of the women in our sample were not planning pregnancies, they might not have been immediately receptive to the folic acid message and, therefore, might have been less likely to currently take folic acid. Moreover, benefits of the intervention could be delayed until women begin to think about pregnancy.

Multivariate analysis demonstrated that women who smoked or used Depo-Provera were twice as likely to be ranked in the lowest quartile of serum folate concentrations than in the highest quartile. Previous research has indicated that smokers have substantially lower serum folate levels than nonsmokers (*9,10*). However, reports of the association between oral contraceptives and serum folate levels are inconsistent (*11,12*), and no study has examined the effects of injectable hormones (e.g., Depo-Provera) on serum folate levels. No substantial difference in serum folate status was identified for women taking oral contraceptives. The findings regarding smoking and contraceptive use might be a reflection of inherent differences among these women (e.g., differences in their metabolic characteristics) as well as related to their behavior.

This analysis also demonstrates that folic acid use, through a folic acid supplement/multivitamin or breakfast cereal, is associated with higher serum folate levels and is an effective method for raising serum folate levels. Misclassification of folic acid consumption could have occurred because asking about folic acid consumption during the previous 2 days could have excluded those women who did not consume folic acid during the previous 2 days but were usually habitual consumers.

TABLE 2. Adjusted* odds ratio for being in the lowest serum folate quartile (≤6.2 ng/mL), compared with the highest quartile (>12.4 ng/mL) among family planning clinic clients — Georgia, 2000

Variable	Lowest 25% (n = 277) Number	%	Highest 25% (n = 264) Number	%	Odds ratio	95% confidence interval
Race						
Black	120	44.1	86	33.1	2.4	1.48, 3.96
White	144	52.9	165	63.5	Ref	—
Age						
18–25	168	61.1	148	56.3	1.1	0.58, 2.15
26–35	74	26.9	71	27.0	1.0	0.51, 2.04
36–45	33	12.0	44	12.0	Ref	—
Education						
Less than high school	54	19.6	34	12.9	1.8	0.98, 3.37
High School or more	221	80.4	230	87.1	Ref	—
Marital status						
Married	64	23.2	63	23.9	1.4	0.85, 2.40
Not married	212	76.8	201	76.1	Ref	—
Contraception method						
Birth control pill	88	33.7	124	50.4	0.9	0.51, 1.74
Depo-Provera®†	83	31.8	37	15.0	2.3	1.15, 4.62
Barrier/withdrawal	31	11.9	30	12.2	1.1	0.48, 2.29
Other	19	7.3	21	8.5	0.7	0.28, 1.75
None	40	15.3	34	13.8	Ref	—
Smoking status						
Any	103	37.5	71	27.0	2.1	1.26, 3.43
None	172	62.6	192	73.0	Ref	—
Multivitamin or folic acid pill use						
Used during last 2 days	23	8.52	85	33.6	0.2	0.09, 0.30
Did not use during last 2 days	247	91.5	168	66.4	Ref	—
Cereal consumption						
Any	80	29.2	135	51.5	0.4	0.26, 0.62
None	194	70.8	127	48.5	Ref	—

* All variables are adjusted for in a single multivariate logistic regression model.
† Contraceptive injection (manufactured by Pharmacia Corporation, Peapack, New Jersey).

However, when controlling for habitual use, defined as taking a multivitamin >4 times during the previous week, similar estimates resulted.

This study is subject to certain limitations. It was designed as part of a folic acid intervention evaluation study and, therefore, questions concerning other behavioral characteristics of the participants were limited. We were unable to collect any information regarding the women's dietary habits other than cereal consumption, which could explain differences in serum folate levels among this group. Other limitations include the low participation rate (60%). Requesting samples of blood might have been a deterrent to participation. The limited sample size limits the conclusions that can be drawn from this study. Further research is needed to determine the reason for these associations between serum folate levels and race, smoking, and injectable contraceptives. Serum folate is a valid measure of folate consumption, but it might not be directly predictive of the risk for NTDs. One strength of the study includes the use of CDC's laboratory that processed both the NHANES 1999 and Georgia blood assays. Using the same laboratory reduced the number of errors resulting from variances in laboratory techniques.

Although serum folate levels have increased in the aggregate national population, certain populations have lower folate levels. Because contraceptive methods are not 100% effective, all women capable of becoming pregnant, regardless of pregnancy intention or current birth control use, should consume adequate amounts of folic acid for preventing NTDs in their children. Targeting specific populations (e.g., women attending family planning clinics) who might be at higher risk for NTDs because of lower folic acid levels can be an effective strategy for continuing to reduce NTDs in the United States.

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Spina Bifida and Anencephaly Prevalence — United States, 1991–2001

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Summary

Spina bifida and anencephaly are serious birth defects. To reduce the occurrence of these birth defects, the Food and Drug Administration authorized the fortification of all enriched cereal grain products with folic acid in March 1996, with compliance mandatory by January 1998. This report reviews data reported to CDC's National Center for Health Statistics (NCHS) regarding spina bifida and anencephaly prevalence for live births in the United States during 1991–2001. Since 1989, NCHS has compiled birth defect data from checkboxes that appear on birth certificates. For consistency in trends, this report uses data for 1991–2001 from all U.S. reporting areas except Maryland, New Mexico, and New York. Data for 2001 are preliminary. During1996–2001, a 23% decline occurred in neural tube defects (spina bifida and anencephaly combined). Spina bifida declined 24% during this period, and anencephaly declined 21%. The United States has experienced declines in spina bifida and anencephaly cases since folic acid fortification of all enriched cereal grain products. The observed declines have translated into approximately 920 infants being born without these serious defects each year. Continued monitoring of the occurrence of spina bifida and anencephaly will be necessary to evaluate the effectiveness of folic acid fortification.

Introduction

In 1992, the U.S. Public Health Service recommended that women of childbearing age increase consumption of the vitamin folic acid to reduce the number of spina bifida and anencephaly cases in the United States (*1*). By 1998, <30% of women were following this recommendation (*2*). In 1996, the Food and Drug Administration (FDA) mandated that all enriched cereal grain products be fortified with folic acid (*3*). An optional period for folic acid cereal grain enrichment started in March 1996, and mandatory fortification began in January 1998. The National Health and Nutrition Examination Survey (NHANES) documented that these public health actions were effective in increasing folate status among U.S. women of childbearing age from NHANES III (1989–1994) to NHANES 1999 (*4*). In 2001, researchers from CDC determined that the overall birth prevalence of these two neural tube defects declined 19% after mandatory folic acid fortification (*5*).

Since 1989, birth certificates in the United States have included 21 checkboxes for birth defects, including spina bifida and anencephaly, and these data are collected by the National Vital Statistics System, a component of CDC's National Center for Health Statistics (NCHS). This system has been a useful data source to determine the effect of folic acid fortification and other sources of folic acid supplementation (*5*).

Methods

NCHS receives birth certificate data collected by state vital statistics offices for the approximately four million births occurring in the United States annually. Data for Maryland, New Mexico, and New York, which had incomplete reporting or did not require reporting for spina bifida and anencephaly for part of the observation period, were excluded from this analysis. This analysis includes trends during 1991–2001 in frequency and prevalence for spina bifida and anencephaly. Included with the birth prevalence are 95% confidence intervals (CI) to determine statistical significance in changes over time. Data for 1991–2000 are final but are preliminary for 2001. The 2001 preliminary data are based on >96% of all births in 2001. More detailed explanations of final and preliminary birth data have been published in other reports (*6,7*).

Results

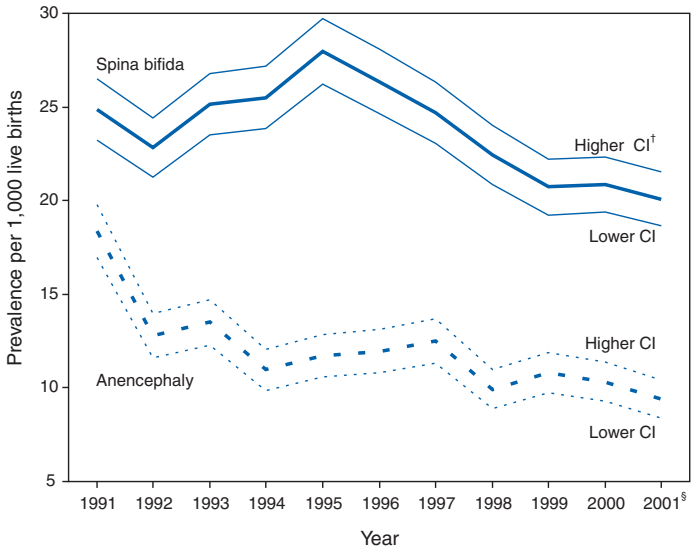
A 23% decline occurred in neural tube defects (spina bifida and anencephaly combined) in 2001, compared with 1996; births in 1996 were conceived before folic acid fortification was authorized. The prevalence of spina bifida reported on birth certificates declined from 24.88 (95% CI = 23.25–26.52) per 100,000 live births in 1991 to 20.09 (95% CI = 18.63–21.54) in 2001 (Table, Figure). The birth prevalences for 1999,

TABLE. Number of live births and prevalence* for spina bifida and anencephaly — United States, 1991–2001†

Year	Spina bifida		Anencephaly		Total no. live births
	No. cases	Prevalence (95% CI§)	No. cases	Prevalence (95% CI)	
1991	887	24.88 (23.25–26.52)	655	18.38 (16.97–19.78)	3,564,453
1992	816	22.84 (21.27–24.41)	457	12.79 (11.62–13.96)	3,572,890
1993	896	25.15 (23.50–26.80)	481	13.50 (12.29–14.71)	3,562,723
1994	900	25.51 (23.85–27.18)	387	10.97 (9.88–12.06)	3,527,482
1995	975	27.98 (26.22–29.74)	408	11.71 (10.57–12.84)	3,484,539
1996	917	26.36 (24.65–28.07)	416	11.96 (10.81–13.11)	3,478,723
1997	857	24.70 (23.05–26.35)	434	12.51 (11.33–13.69)	3,469,667
1998	790	22.45 (20.88–24.01)	349	9.92 (8.88–10.96)	3,519,240
1999	732	20.72 (19.22–22.22)	382	10.81 (9.73–11.89)	3,533,565
2000	759	20.85 (19.37–22.33)	376	10.33 (9.28–11.37)	3,640,376
2001¶	733	20.09 (18.63–21.54)	343	9.40 (8.40–10.39)	3,649,061

* Per 100,000 live births.
† Excludes data for Maryland, New Mexico, and New York, which did not require reporting for spina bifida and anencephaly for certain years.
§ Confidence interval.
¶ Data for 2001 are preliminary.
Source: National Vital Statistics System, National Center for Health Statistics, CDC.

FIGURE. Spina bifida and anencephaly prevalence — United States, 1991–2001*



* Excludes data for Maryland, New Mexico, and New York, which did not require reporting for spina bifida and anencephaly for certain years.
† 95% confidence interval.
§ Data for 2001 are preliminary.
Source: National Vital Statistics System, National Center for Health Statistics, CDC.

2000, and 2001 were significantly lower than in 1996 (pre-fortification). The 2001 prevalence was 24% lower than the prevalence in 1996; after a significant increase in the prevalence during 1992–1995, a significant decline occurred during 1995–1998. The birth prevalence of spina bifida was stable during 1999–2001. The prevalence of anencephaly reported on birth certificates declined from 18.38 (95% CI = 16.97–19.78) per 100,000 live births in 1991 to 9.40 (95% CI = 8.40–10.39) in 2001. After a decline in the early part of the decade, the anencephaly prevalence was stable during the mid-1990s. The prevalence of anencephaly in 2001 was 21% lower than in 1996. The birth prevalence did not change significantly during 1998–2001, the period of optional and mandatory folic acid fortification.

Discussion

Spina bifida and anencephaly are serious birth defects that occur when the neural tube fails to close properly during fetal development. Anencephaly is a lethal defect, and spina bifida results in serious long-term morbidity and disability. Before folic acid fortification, approximately 4,000 pregnancies resulted in 2,500–3,000 births in the United States each year affected by one of these two neural tube defects (*1,8*)

U.S. birth certificate data in this report demonstrate a 24% decline in spina bifida in 2001 births (based on preliminary data) compared with the occurrence of spina bifida in 1996 (before folic acid fortification). A decline of 21% in anencephaly was observed during the same period. This decline is similar to those observed by using the first 5 quarters postfortification, which was previously published (*5*).

Although prevalence for birth defects (including spina bifida and anencephaly) as reported from birth certificate data has been underreported, the collection over time is considered to be stable (*5,9*). Further support of the findings from birth certificate data has come from population-based surveillance systems. Data from 24 birth defect surveillance systems indicated a 31% decline in spina bifida and a 16% decline in anencephaly when comparing the postfolic acid fortification years (October 1998–December 1999) with the pre-fortification years (January 1995–December 1996) (*10*).

Nine of these birth defect surveillance systems ascertain defects that are prenatally diagnosed and terminated, allowing them to capture additional defects. Larger declines after folic acid fortification were observed for both spina bifida and anencephaly when analysis was limited to these nine surveillance systems with enhanced ascertainment (*10*).

Maryland and New York were excluded in this report to provide consistent trend data, because they only began reporting both spina bifida and anencephaly in 1996. The inclusion of data from these two states does not have a significant effect on the overall prevalence for spina bifida or anencephaly, nor does it change the direction or pattern of change in the trend. New Mexico data are not available because the state does not require reporting of these defects on birth certificates.

The declines observed in both birth certificate data and birth defects surveillance system data are less than the decline of ≥50% that was predicted on the basis of certain observational studies (*1*). Possible explanations for this difference include 1) the majority of folate-preventable neural tube defects in the United States might have been eliminated before fortification or 2) subpopulations of U.S. women might have not received adequate folic acid from either folic acid fortification or folic acid supplementation. Alternatively, the findings from the observational studies might not be applicable to populationwide interventions (e.g., folic acid fortification), possibly because of biases or uncontrolled confounding that might have been present in the observational studies.

The 23% decline in neural tube defects (spina bifida and anencephaly combined) indicated by birth certificate data translates to approximately 920 additional babies without neural tube defects being born in the United States each year. Although this decline represents a lower reduction than those predicted on the basis of earlier studies, by September 2002, neural tube defects will have been prevented in nearly 4,000 U.S. children after folic acid fortification. Attaining and sustaining these substantial declines in neural tube defects is an important public health achievement.

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Sociodemographic Patterns in Spina Bifida Birth Prevalence Trends — North Carolina, 1995–1999

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Summary

Previous studies have documented a decline in neural tube defects (NTDs) in the United States after the addition of folic acid to enriched grain products and other folic acid initiatives. The decrease generally has been greater for spina bifida than for other NTDs. However, the extent to which the decline varies by maternal sociodemographic characteristics has not been examined. In this study, data from the North Carolina Birth Defects Monitoring Program, a statewide, population-based birth defect surveillance program, were used to assess the impact that folic acid public health initiatives have had on spina bifida rates among various sociodemographic subpopulations in North Carolina. This report covers data from 1995 through 1999. The overall prevalence of spina bifida decreased by 27.2% during 1995–1996 and 1998–1999 (p = 0.014). The magnitude of the decline varied considerably by sociodemographic characteristics of the mother. The decline was greatest among mothers who were aged ≥30 years (prevalence ratio [PR] = 0.53), who had more than a high school education (PR = 0.57), whose prenatal care was not paid by Medicaid (PR = 0.67), and who were non-Hispanic white (PR = 0.72). Geographically, the decrease in the western and Piedmont regions of the state was almost threefold that occurring in the eastern region. The decline in spina bifida after fortification varied considerably by sociodemographic subpopulations. More effort is needed to target folic acid education programs at disadvantaged populations.

Introduction

Previous studies have demonstrated a decline in the birth prevalence of spina bifida after the addition of folic acid to enriched grain products and the initiation of folic acid education programs during the 1990s. An analysis of birth certificate data in the United States found that the rate of spina bifida declined 16% during 1991–2000 (*1*). A subsequent study using U.S. birth certificate data documented a 23% decline in spina bifida after fortification (*2*), and a recent analysis of data from 24 state birth defects surveillance programs also demonstrated a decline in spina bifida prevalence since the mid-1990s (*3*). Although the findings of these studies demonstrate that spina bifida has declined in the years following fortification, the extent to which this decline varies by sociodemographic characteristics has not been assessed. This report describes the association between maternal sociodemographic factors and recent trends in spina bifida in North Carolina. This information can be helpful for assessing the effects that folic acid initiatives have had on various segments of the population and for identifying subgroups for which targeted educational activities are most needed.

Methods

Case Definition and Ascertainment

Cases of spina bifida were identified from the North Carolina Birth Defects Monitoring Program (NCBDMP). The NCBDMP is a statewide, population-based surveillance system that collects information on congenital malformations diagnosed within the first year of life among North Carolina resident liveborn infants and among stillborn infants aged ≥20 weeks' gestation. The surveillance system covers a birth population of >110,000 deliveries annually. Beginning with births occurring in 1995, the NCBDMP initiated an enhanced system for ascertaining infants with neural tube defects (NTDs). Trained case abstractors conducted routine visits at the state's 12 tertiary hospitals to review medical records and abstract information about infants suspected of having NTDs or other birth defects. Suspected cases were identified through reviewing hospital disease indexes and through genetics and prenatal diagnosis logs in selected hospitals. Data sources used to identify cases at non-tertiary hospitals include hospital discharge data, vital statistics, and Medicaid paid claims files. All suspected NTD cases were confirmed through chart review.

Cases of spina bifida were defined according to *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) codes 741.00–741.93 (*4*) and included those affecting all resident liveborn infants and stillborn infants aged ≥20 weeks' gestation delivered during 1995–1999. A total of 299 spina bifida cases were identified during the 5-year study period, resulting in 279 live births and 20 fetal deaths.

Data Analysis

Cases were matched with the North Carolina composite matched birth files for 1995–1999. This database contains information extracted from vital statistics files (matched birth and infant death certificates), Medicaid paid claims, and other health services-related data for all North Carolina resident births. The prevalence of spina bifida (number of cases per 10,000 births) for each year was calculated overall and for the following maternal characteristics: age, race, education, Medicaid status (as defined by whether the delivery was paid for by Medicaid), and geographic area of residence.

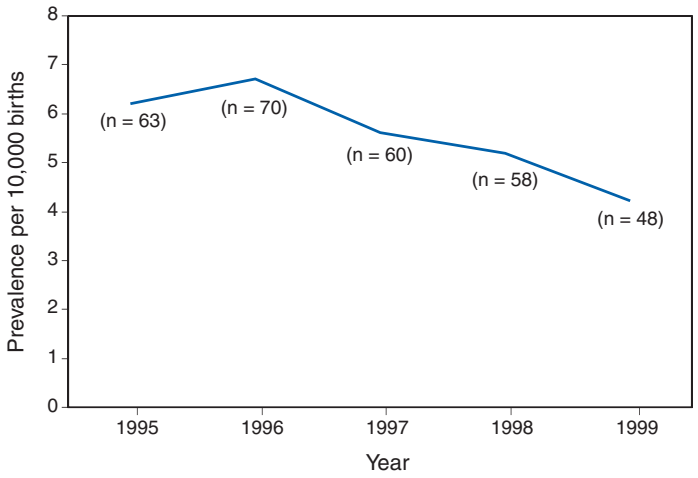
Poisson regression was used to examine the overall trend in the spina bifida prevalence during 1995–1999. This method is appropriate for modeling disease incidence data in which the event (numerator) is relatively rare in proportion to the total population at risk (*5*). A Poisson log-linear model was fitted to the data by using SAS PROC GENMOD (*6*), modeling the change in rates as a function of year. To assess whether the change in prevalence varied according to maternal characteristics, the prevalence for the most recent 2-year period (1998–1999) was compared with that of the earliest period (1995–1996) for each of the previously described sociodemographic variables. Prevalence ratios (PR) and 95% confidence intervals (CI) were computed to compare the two time periods.

Results

The number of spina bifida cases in North Carolina declined from 63 in 1995 to 48 in 1999, despite the 12% increase in the total number of live births in the state during this period. During 1995–1999, the overall prevalence of spina bifida declined by 32% (p = 0.015, based on Poisson regression), from 6.20/10,000 live births in 1995 to 4.22/10,000 in 1999 (Figure).

Comparing the earliest and most recent 2-year periods (1995–1996 and 1998–1999), the overall spina bifida prevalence declined by 27.2% (PR = 0.73, 95% CI = 0.56–0.94). However, the magnitude of the decrease differed substantially according to maternal characteristics (Table). The greatest declines were seen among mothers in the older age groups,

FIGURE. Prevalence (per 10,000 live births) of spina bifida by year — North Carolina, 1995–1999



especially women aged ≥30 years, in which the prevalence decreased by 47.0% (PR = 0.53, 95% CI = 0.33–0.84). In contrast, among women aged <25 years, the prevalence remained virtually unchanged (PR = 0.99, 95% CI = 0.67–1.45). The spina bifida prevalence for women with more than a high school education declined by 43.2% (PR = 0.57), which was about 2.5 times the amount of decline observed among women with a high school education or less. Among women whose prenatal care was not paid by Medicaid, the prevalence declined by about one third (PR = 0.67), compared with an 18.5% decrease for women receiving Medicaid. Differences in the decrease in spina bifida by race were less marked, although the decline among white non-Hispanic mothers was slightly greater compared with the decline among minority women (PR = 0.72 and 0.76, respectively). Geographic differences also were observed in the decline of spina bifida; decreases in western North Carolina and in the Piedmont region were nearly threefold those experienced in the East.

Discussion

The decrease in the rate of spina bifida since the mid-1990s is consistent with previous reports that have demonstrated similar declines in the United States (*1–3*). However, this study reveals that the reduction in spina bifida in North Carolina was not uniform across the population, but varied by geographic region as well as by maternal sociodemographic characteristics. The decline was generally greater among women who tend to be of higher socioeconomic status (i.e., those who are older, have higher education, and are not receiving Medicaid. The decrease was also considerably greater in the western and Piedmont regions of the state compared with the eastern coastal plain, a pattern that reflects the sociodemographic

TABLE. Prevalence of spina bifida (per 10,000 live births) by selected maternal characteristics — North Carolina, 1995–1996 and 1998–1999

Characteristic	1995–1996 No.	1995–1996 Prevalence (per 10,000 births)	1998–1999 No.	1998–1999 Prevalence (per 10,000 births)	Prevalence ratio	95% CI*
Mother's age						
<25 years	52	5.91	54	5.83	0.99	0.67–1.45
25–29 years	34	6.11	24	3.83	0.63	0.37–1.06
≥30 years	47	7.55	28	3.99	0.53	0.33–0.84
Mother's education						
High school or less	85	7.43	75	6.18	0.83	0.61–1.13
Beyond high school	42	4.61	27	2.62	0.57	0.34–0.92
Mother's race						
White/non-Hispanic	95	7.00	72	5.04	0.72	0.53–0.98
Other	38	5.41	34	4.12	0.76	0.48–1.21
Mother's Medicaid status						
Medicaid	70	7.18	60	5.86	0.82	0.58–1.15
Non-Medicaid	53	4.88	40	3.25	0.67	0.44–1.00
Geographic region						
Western	30	8.67	21	5.63	0.65	0.37–1.13
Piedmont	62	6.03	47	4.05	0.67	0.46–0.98
Coastal Plain	41	5.99	38	5.28	0.88	0.57–1.37
Total	**133**	**6.46**	**106**	**4.70**	**0.73**	**0.56–0.94**

* Confidence interval.

differences among these regions. In addition, western North Carolina was the first area of the state to initiate a well-coordinated and intensive folic acid education program; this effort may have contributed to the dramatic decline observed in that region.

Much of the recent decline in NTDs in the United States has been attributed to the mandatory fortification program rather than to increased intake of multivitamins. Data from the March of Dimes/Gallup surveys indicate that the percentage of women aged 18–44 years who take daily multivitamins has increased only slightly since 1995 (*7*). In addition, preliminary data from the National Health and Nutrition Examination Survey (NHANES) IV indicate that supplement use among women of childbearing age was similar to that reported among women participating in the NHANES III survey; yet, blood folate levels increased significantly during the 5 years between the two surveys (*8*). As indicated by the present study, however, the fortification program in the United States may not have benefited all segments of the population equally. One explanation is that sociodemographic differences in food consumption patterns and multivitamin intake may be mediating the effect that fortification is having in various subpopulations.

Some nationally representative studies have documented differences in consumption patterns of enriched grain products by sociodemographic characteristics. For example, persons with higher income, those with more education, and non-Hispanic whites tend to consume more cereals (*9–12*). These differences in cereal consumption are noteworthy because of the now widespread availability of ready-to-eat breakfast cereals that are fortified at 100% of the recommended daily value. Furthermore, total folate intakes are higher among non-Hispanic white and black women in the middle and upper socioeconomic classes compared with the lowest (US Department of Agriculture. Continuing Survey of Food Intake by Individuals, 1994–1996, unpublished data). Although more studies are needed to determine whether these food consumption patterns persist in the postfortification era, the data that are available correlate with the sociodemographic trends in spina bifida reported in this study.

Like dietary patterns, multivitamin use also differs by sociodemographic characteristics (*13–15*). Several studies demonstrate that older, higher income, non-Medicaid, and better educated women are more likely to be taking supplements. The greatest declines in spina bifida have occurred among infants born to women of these same sociodemographic groups.

Folic acid fortification might be having a greater effect in reducing NTD risk among those women whose nutritional status is already near an optimal level, e.g., women who are more likely to consume ready-to-eat cereals, to take multivitamins on an occasional basis, and to maintain a more well balanced diet. The current fortification level has been estimated to increase the average woman's consumption of folic acid by about 100 µg per day (*16*). Although this amount is only about one fourth of the total intake recommended by CDC for birth defects prevention, it may be sufficient for women whose baseline folates were already at or above the prefortification median levels. For these women, fortification may have

provided sufficient additional folic acid in their diets to raise their folate levels to the optimal threshold needed to prevent birth defects. Such women tend to be from more affluent sociodemographic populations. In contrast, among women from more disadvantaged groups who tend to be in poorer nutritional status and are less likely to take any multivitamins, the current fortification level might be considerably less than the amount needed for full birth defects prevention.

The possibility that the recent decline in spina bifida is only part of a secular trend in the prevalence of NTDs cannot be ruled out. Throughout much of the world, the rate of NTDs has been declining during the past several decades (*17*), and to some extent, the decrease seen in recent years can be viewed as a continuation of that trend. In this context, gauging the extent to which folic acid interventions may have contributed to the recent decline is difficult. Nevertheless, the increase in blood folate levels in the United States, combined with evidence of concomitant decrease in NTDs from multiple studies, supports the view that folic acid initiatives are contributing to the prevention of NTDs.

The extent to which the recent decline in spina bifida and other NTDs may be attributed to mandatory fortification, increased multivitamin intake, or increased availability of fully fortified, ready-to-eat cereals cannot be assessed with the data available. Most likely, all these factors combined have led to the dramatic improvements seen in recent years and help explain why certain segments of the population have benefited more than others.

Additional studies using data from population-based birth defect surveillance programs are needed to confirm the results of this study. The present findings indicate that substantial potential still exists for further reductions in spina bifida, particularly among minorities and women of lower socioeconomic status. With the effects of the fortification program probably having already been realized, sustaining the decline will require more aggressive efforts to encourage minority women of childbearing age, as well as those from lower socioeconomic groups, to take daily multivitamins containing 400 µg of folic acid in addition to eating a well-balanced, folate-rich diet.

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Folic Acid Awareness and Use Among Women with a History of a Neural Tube Defect Pregnancy — Texas, 2000–2001

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Summary

The use of folic acid is a critical component in preventing birth defects. Health-care providers should take advantage of all health-care visits to counsel not only women at high risk (i.e., those with a history of having an infant with a neural tube defect [NTD]) but all women regarding the importance of folic acid use. A study conducted in Texas confirmed that white and Hispanic mothers were equally likely to recall receiving postpartum advice to use folic acid; however, Hispanic women were much less likely to use folic acid, compared with white women. This report covers data from May 2000 through November 2001. A study was conducted in Texas to determine whether women at high risk recall and follow recommendations to use folic acid. The study included 195 women at high risk and 223 control mothers who gave birth to infants without birth defects. These women participated in a telephone interview for a population-based case-control study of NTDs. Approximately 56.4% (110 of 195) of mothers who had infants affected by an NTD recalled receiving postpartum advice to use folic acid, compared with 25.6% (57 of 223) of control mothers ($p < 0.01$). Among nonpregnant case mothers, 54 (32.7%) of 165 reported regular use of supplements containing folic acid, and 53 (25.2%) of 210 nonpregnant control mothers reported this behavior ($p = 0.11$). Among case mothers, use of folic acid was significantly higher for whites (64.7%) versus Hispanics (16.5%) ($p < 0.001$); for women with some college education (57.1%) versus no college education (20.2%; $p < 0.001$); for women who were trying to get pregnant (66.7%) versus those using birth control (38.3%) or reporting using no contraceptive method (18.8%) ($p = 0.001$); and for women who reported receiving advice to use folic acid (40.9%) versus those who did not (22.2%; $p = 0.01$). Findings from this study support the need to implement NTD recurrence prevention activities in Texas. Data also identify a need for educational strategies in Texas that target Hispanic women at high risk, especially those who primarily speak Spanish. Further efforts should be made to determine why Hispanic women have low rates of folic acid use (e.g., the cost of vitamins and language and cultural barriers). On the basis of a review of research and current practice, recommendations developed by the Public Health Service include 1) women at risk for a recurrent NTD-affected pregnancy should take 0.4 mg of folic acid per day; and 2) if a woman at high risk is planning a pregnancy, she should consult her physician regarding taking the higher dose of 4.0 mg per day.

Background

For women who previously have had a neural tube defect (NTD)-affected infant, the risk for having another is 1%–3%, or 10–30 times the risk among the general population (*1,2*). From 1993 through 1999, a CDC-funded, population-based intervention study of these women at high risk was conducted among a primarily Hispanic population residing in Texas counties bordering Mexico (*3*). The success of this intervention indicated that NTD recurrence prevention activities should possibly be expanded in Texas. To determine the need for statewide NTD recurrence prevention, this statewide study was conducted to assess awareness and supplementation practices among women who recently delivered NTD-affected infants.

Methods

This study is an add-on component to the National Birth Defects Prevention Study, a multistate, case-control study of risk factors for 35 major birth defects sponsored by CDC (*4*). Eight states, including Texas, participated in the study, using a standardized, 60-minute, computer-assisted telephone interview and informed consent. In Texas, mothers who participated in the national interview and who had children with

NTDs (i.e., spina bifida and anencephaly) were invited to participate in an additional 20-minute interview (Texas Interview for Prevention of Central Nervous System Birth Defects [TIP-CNS]). The current study includes 195 mothers of infants with NTDs and 223 control mothers who participated in both of these interviews. All data regarding folic acid awareness and use of folic acid at the time of the interview derived from the TIP-CNS interview.

Telephone interviews for the study participants were conducted during May 2000–November 2001. Eligible women were contacted by telephone and invited to participate in the interview, which was administered in English or Spanish. The median time between delivery or pregnancy termination and the interview was 15 months (range: 3.4 months–34.4 months) for case mothers and 14.1 months (range: 1.4 months–32.9 months) for control mothers. Estimated participation rates were 57% (195 of 342) for case mothers and 51% (223 of 437) for control mothers.

Cases were ascertained by the population-based Texas Birth Defects Monitoring Program, an active surveillance system for all birth defects diagnosed among elective pregnancy terminations, fetal deaths, live births, and infants (aged <1 year) (*5*). Cases were identified by an active search of medical records in all hospitals in Texas. Chromosomal abnormalities and syndromes are ascertained by the monitoring program but were not included in this study. Controls were live infants without malformations who were randomly selected from the same Texas hospitals from which the cases were ascertained, in proportion to the live birth proportion contributed by that hospital during the previous year.

Women who stated that they took folic acid or multivitamins the majority of days or every day were considered to be regular users of folic acid supplements. Women who responded that they took folic acid occasionally or never were classified as nonusers.

Results

Mothers of infants affected by NTDs were much more likely to remember receiving postpartum advice to use folic acid from a physician or health-care worker, (n = 195; 56.4%), compared with control mothers, (n = 223; 25.6%; $p < 0.01$) (Table 1). Recall of advice regarding folic acid among case mothers did not differ by type of defect, race/ethnicity, education, pregnancy/contraceptive status, or outcome of pregnancy. Demographic patterns (e.g., race/ethnicity and education) for recall among control mothers were similar to those for case mothers.

To determine the proportion of women who were complying with the recommendation to use folic acid before they become pregnant, women who were pregnant at the time of

TABLE 1. Proportion of mothers who recall having received postpartum advice to use folic acid — Texas, 2000–2001

	Mothers of infants with NTD*			Control mothers†		
Category	**Yes/Total**	**(%)**	**P value**	**Yes/Total**	**(%)**	**P value**
Spina bifida	61/110	(55.5)	0.76	—	—	—
Anencephaly	49/85	(57.6)	—	—	—	—
Race/Language						
White/English	42/67	(62.7)	0.63	24/82	(29.3)	0.78
Hispanic/English	29/53	(54.7)	—	16/66	(24.2)	—
Hispanic/Spanish	29/56	(51.8)	—	11/46	(23.9)	—
Other/English	10/19	(52.6)	—	6/29	(20.7)	—
Education						
≤High school graduate	70/125	(56.0)	0.88	29/130	(22.3)	0.19
Some college or college graduate	40/70	(57.1)	—	28/93	(30.1)	—
Age group (yrs)						
≤18	8/16	(50.0)	0.004	2/13	(15.4)	0.62
18–29	83/129	(64.3)	—	38/149	(25.5)	—
≥30	18/49	(36.7)	—	17/60	(28.3)	—
Contraceptive status						
Currently pregnant	17/30	(56.7)	0.94	3/13	(23.1)	0.87
Trying to get pregnant	9/15	(60.0)	—	1/7	(14.3)	—
Using birth control	47/81	(58.0)	—	23/83	(27.7)	—
Other	37/69	(53.6)	—	30/120	(25.0)	—
Outcome						
Live birth	62/120	(51.7)	0.12	57/223	(25.6)	§
Fetal death	13/24	(54.2)	—	0/0	(00.0)	—
Induced abortion	35/51	(68.6)	—	0/0	(00.0)	—
Total	**110/195**	**(56.4)**	—	**57/223**	**(25.6)**	—

* Neural tube defects.
† No birth defects occurred among controls.
§ Controls are comprised of live births only.

TABLE 2. Proportion of nonpregnant mothers who reported taking folic acid regularly — Texas, 2000–2001

	Mothers of infants with NTD*			Control mothers†		
Category	**Yes/Total**	**(%)**	**P value**	**Yes/Total**	**(%)**	**P value**
Spina bifida	29/99	(29.3)	0.25	—	—	—
Anencephaly	25/66	(37.9)	—	—	—	—
Race/Language						
White/English	33/51	(64.7)	<0.001	33/77	(42.9)	<0.001
Hispanic/English	9/45	(20.0)	—	11/63	(17.5)	—
Hispanic/Spanish	7/52	(13.5)	—	4/44	(9.1)	—
Other/English	5/17	(29.4)	—	5/26	(19.2)	—
Education						
≤High school graduate	22/109	(20.2)	<0.001	20/124	(16.1)	<0.001
Some college or college graduate	32/56	(57.1)	—	33/86	(38.4)	—
Age group (yrs)						
≤18	1/12	(8.3)	0.13	1/12	(8.3)	0.25
18–29	40/110	(36.4)	—	35/142	(24.6)	—
≥30	13/43	(30.2)	—	17/55	(30.9)	—
Contraceptive status						
Trying to get pregnant	10/15	(66.7)	0.001	2/7	(28.6)	0.98
Using birth control	31/81	(38.3)	—	21/83	(25.3)	—
Other	13/69	(18.8)	—	30/120	(25.0)	—
Outcome						
Live birth	31/106	(29.2)	0.42	53/210	(25.5)	§
Fetal death	8/19	(42.1)	—	0/0	(00.0)	—
Induced abortion	15/40	(37.5)	—	0/0	(00.0)	—
Advised to use folic acid						
Yes	38/93	(40.9)	0.01	20/54	(37.0)	0.02
No	16/72	(22.2)	—	33/156	(21.2)	—
Total	**54/165**	**(32.7)**	—	**53/210**	**(25.2)**	—

* Neural tube defects.
† No birth defects occurred among controls.
§ Controls are comprised of live births only.

the interview were excluded from the analyses (Table 2). Among nonpregnant case mothers, 54 (32.7%) of 165 reported regular use of multivitamins or folic acid at the time of the interview, compared with 53 (25.2%) of 210 control mothers. Among nonpregnant case mothers, regular use of folic acid or multivitamins varied substantially across ethnic groups: 33 (64.7%) of 51 white women, 9 (20.0%) of 45 English-speaking Hispanic women, and 7 (13.5%) of 52 Spanish-speaking Hispanic women ($p < 0.001$) (Table 2). A similar difference was observed among nonpregnant control women, ($p < 0.001$) (Table 2). Among nonpregnant case and control mothers, those with some college education were more than twice as likely to use folic acid regularly than those with no college education ($p < 0.001$ for case and control mothers) (Table 2). In addition, both case and control mothers who reported having received postpartum advice to use folic acid were nearly twice as likely to be taking supplemental folic acid at the time of the interview, compared with mothers who did not recall such advice ($p = 0.01$ for case mothers; $p = 0.02$ for control mothers).

Nonpregnant case mothers who reported that they were trying to get pregnant were much more likely to report regular use of folic acid: 10 (66.7%) of 15 were regular users, compared with 31 (38.3%) of 81 women using birth control, and 13 (18.8%) of 69 women who did not use birth control ($p = 0.001$) (Table 2). This last category includes women who were sexually inactive and women who were sexually active but elected not to use birth control. The interview questions did not distinguish between these two categories. In contrast, among control mothers, the corresponding rates were not significantly different; rates were 28.6%, 25.3%, and 25.0%, respectively ($p = 0.98$).

Recall of receiving advice to use folic acid did not vary by time between delivery and interview (categories examined: 1–6 months, 7–12 months, 13–18 months, and 19–35 months). Therefore, time from interview is not likely to be a bias in our results. No appreciable change occurred in these findings after adjustment for maternal age, ethnic group, educational level, contraceptive status, pregnancy outcome, and case-control status.

Discussion

Of study subjects who had a previous NTD-affected pregnancy, 43% did not recall receiving advice regarding taking folic acid supplements of any type, and only approximately

one third (32.7%) of nonpregnant subjects were using folic acid supplements regularly. Given the 1%–3% level of risk for NTD recurrence among this population, the percentage of women receiving this counseling must be improved. Other studies based on different methods have reported similar findings (*6*–*9*).

This survey has certain limitations. The participation rates in this study were low, but they were similar to those of other recently conducted case-control studies (*10*). Women of lower educational status might be underrepresented, because they move more often and are less likely to have a telephone. They also have lower rates of awareness and use of folic acid (*11*). Therefore, rates of awareness and use of folic acid among all women in Texas with NTD-affected pregnancies might be lower than the rates in this report. In addition, differences across ethnic groups might be larger than the differences in this report.

Health-care providers should take advantage of all health-care visits to counsel not only women at high risk but all women regarding the importance of folic acid use. Although white mothers and Hispanic mothers were equally likely to recall receiving postpartum advice to use folic acid, Hispanic women were much less likely to use folic acid, compared with white women. Therefore, further efforts should be made to explore the reasons that Hispanic women have such low rates of folic acid use, including the cost of vitamins and language and cultural barriers.

A substantial number of unintended pregnancies occur among women using hormonal contraceptives (*12*). Therefore, women should be advised to take folic acid every day regardless of whether they use contraceptives. Women who were not trying to become pregnant and were not using contraception were the least likely to use folic acid. Reaching these women is vital, because they have a high risk of becoming pregnant and because, on average, their economic status is lower (*12*), placing them at a higher risk for having an infant with an NTD (*13*).

The low rates of awareness and use of folic acid among women at high risk and the complex decision-making processes involved in reproductive health support the need for programs to identify women at high risk and to counsel them regarding folic acid use. Such programs use educational approaches specifically tailored for women at high risk and are a key adjunct to counseling by physicians and other health-care providers. These findings are important to consider as Texas develops its statewide NTD recurrence prevention strategy.

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