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An analysis of folic acid supplementation in women presenting for antenatal care

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ABSTRACT

Background Neural tube defects (NTDs) are major congenital malformations that are potentially preventable if the woman takes periconceptional folic acid (FA) supplements. A recent report found that NTD incidence had increased in Ireland. This study examined the usage of FA supplementation in women presenting for antenatal care in a maternity hospital.

Methods Women were recruited at their convenience in the first trimester. Their clinical and sociodemographic details were computerized. Maternal weight and height were measured before calculating body mass index. Detailed FA questionnaires were completed under supervision of a trained researcher.

Results While 96.1% ($n = 564$) out of 587 reported that they took FA after they became pregnant, only 24.7% ($n = 145$) took it for >12 weeks preconceptionally as recommended. Only 5.7% ($n = 6$) of obese women took high-dose FA as recommended. On univariate analysis, the strongest predictors of preconceptional FA usage were higher maternal age, higher education and income, being married, being nulliparous, not smoking, infertility treatment and planned pregnancy. On multivariate analysis, both planned pregnancy and nulliparity were the most important predictors of preconceptional FA use.

Conclusions Our study shows that current recommendations to prevent NTDs by FA supplementation pre-pregnancy are not being fully implemented in Ireland. We recommend a review of current public health policies on FA supplementation.

Keywords folic acid supplementation, Ireland, neural tube defects, planned pregnancy

Introduction

Neural tube defects (NTDs) arise due to incomplete closure of the neural tube within a month of conception.[1] Anencephaly is incompatible with life. Spina bifida and encephalocoele both have a high perinatal and infant mortality. Although 80% of infants with spina bifida survive, the condition is associated with varying degrees of physical disability. Ireland has a higher rate of NTDs than other European countries.[2] A recent study has also shown that the incidence rates of NTDs in the Republic of Ireland have increased significantly from 0.92/1000 in 2005–06 to 1.17/1000 in 2009–11.[3] Furthermore, in Ireland, the majority of babies with spina bifida are live-born, and thus, the burden of illness is heavy for the individuals and their families. In economic terms, the direct and indirect costs are also high for the individual affected and for the health services.[4]

In the early nineties, two landmark papers were published which showed that periconceptional folic acid (FA) supplementation can prevent >70% of NTDs.[5,6] Following this, a number of recommendations were made to promote FA

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supplementation among women of childbearing age.[7,8] There is little consistency between guidelines on the duration of supplementation before pregnancy. Some recommend that FA supplementation should be commenced 1 month preconceptionally[7] while others recommend that it is taken for at least 12 weeks before conception.[9] Other guidelines make no reference to the duration of preconceptional FA recommended and instead recommend that FA is commenced once a woman starts to plan a pregnancy.[10] However, the scientific evidence indicates that it takes an average of 12 weeks of supplementation with 400 μg FA to achieve the desired red cell folate (RCF) level of 906 nmols.[11] This is the level of RCF associated with a reduced risk of NTDs.[12] Thus, ideally women should take FA for at least 3 months before conception. There is also evidence that the incidence of NTDs is increased in women who are obese.[13,14] International guidelines, therefore, recommend that obese women should take high-dose (5 mg) FA periconceptionally to reduce their risk of NTDs.[15–17] However, no intervention or observational studies specifically address prevention of NTDs in obese women.

There is limited contemporary information on FA uptake before pregnancy in the obstetric population. There is also a specific lack of information on the use of high-dose FA supplementation, particularly in obese women. The purpose of this prospective observational study was to analyse in detail the use of FA supplementation in women presenting for antenatal care in a large Irish maternity hospital.

Methods

The Coombe Women and Infants University Hospital is one of the largest maternity hospitals in the European Union and cares for women from all socioeconomic groups and across the urban–rural divide. The demographics of the women who attend are similar to the national population.[18] The woman's clinical and sociodemographic details are computerized routinely at the first antenatal visit and updated immediately after delivery. The inclusion criteria for this study were women booking for antenatal care after an ultrasound examination confirmed an ongoing singleton pregnancy in the first trimester. The exclusion criteria were multiple pregnancies, women <18 years and a woman's inability to understand English.

Women were recruited using convenience sampling by the trained research dietitian at their first antenatal visit before 18 weeks of gestation after sonographic confirmation of a normal ongoing pregnancy. If the woman agreed to participate in the study they were administered the relevant questionnaires. The questionnaire was completed in-person under the supervision of the trained research dietitian, taking ∼20 min to complete.

Folic acid questionnaire

A detailed FA questionnaire was completed under the supervision of the research dietitian to collect information on FA supplementation. The questionnaire included questions about the use of FA both pre- and periconceptionally, as well as data on the dose and brand name of FA used, compliance with FA supplement use guidelines, and maternal characteristics such as socioeconomic information, level of education, smoking status and number of years spent living in Ireland.

Anthropometric data

Height was measured to the nearest centimetre using a Seca wall-mounted digital metre stick with the woman standing in her bare feet. Weight was measured digitally and body mass index (BMI) calculated. Written informed consent was obtained. The study was approved by the Hospital's Research Ethics Committee.

Information on socioeconomic status was derived using questions from the Survey on Income and Living Conditions.[19] Material indices of disadvantage including 'at risk of poverty' and relative deprivation status were assessed, while consistent poverty status was also calculated. 'At risk of poverty' status was determined by comparing equalized household income against the 60% median income threshold. Relative deprivation was assessed by determining whether the respondents had experienced enforced absence (due to financial constraint) of 2 or more basic necessities from a list of 11. Consistent poverty was identified if a respondent reported being 'at risk of poverty' in addition to experiencing enforced absence of 2 or more of the 11 basic markers of deprivation.[19] The detailed algorithmic methods used for the calculation of these indicators are available in a document produced by the European Commission.[20] This methodology is currently used by the Irish Central Statistics Office to calculate material indices of disadvantage such as 'at risk of poverty'.[19]

Statistical analysis

Data from the participants' questionnaires were anonymized and coded on a Microsoft Excel© spreadsheet. Appropriate continuous variables were collapsed into categorical variables. The distribution of continuous data was assessed for normality by assessing the kurtosis and skewness of the distribution and the associated Kolmogorov–Smirnoff statistics, and by a visual inspection of the distribution histogram and box plot.

Descriptive statistics were first used to describe the characteristics of the study cohort. Inferential χ^2 tests for independence

were then used to analyse differences in categorical variables (use of FA supplementation preconceptionally, FA supplementation for >12 weeks preconceptionally) between different population groups.

Binary logistic regression analyses were finally performed to assess the independent association of a number of putative predictor variables with the likelihood of using preconceptional FA. Factors were included in the multivariate model based on a statistically significant finding from the univariate analyses ($P < 0.05$). Two regression models were constructed: one examining the use of FA before pregnancy, and one examining compliance with the guideline for FA supplementation for >12 weeks preconceptionally. The first model included eight independent variables, each selected due to its significant association with preconceptional FA use upon univariate analysis ($P < 0.05$). In the second model examining compliance with the guideline for FA supplementation >12 weeks preconceptionally, eight independent variables were included, again based on their significant association with this outcome variable upon univariate analysis. A *P*-value of <0.05 was considered statistically significant.

Results

The characteristics of the women interviewed ($n = 587$) are shown in Table 1. Twenty-four women refused to participate because of time constraints, e.g. they had to return to work. The demographics of the total study population were similar to the hospital population.[18] Overall, 18.1% of the women ($n = 106$) were obese based on a BMI of ≥30 kg/m^2.

The usage of FA supplementation is shown in Table 2. Only 24.7% ($n = 145$) took FA for >12 weeks before conception.[9,11] Of the 564 women who reported taking FA at any point during their pregnancy, only 2.7% ($n = 15$) reported taking high-dose FA supplementation. The reasons given for taking high-dose FA were epilepsy ($n = 6$), diabetes mellitus ($n = 2$), obesity ($n = 2$) and assisted reproduction ($n = 2$) and other reasons ($n = 3$).

Table 3 shows the characteristics of the women who took FA preconceptionally and of the women who supplemented for >12 weeks preconceptionally as recommended. It shows that women who complied with preconceptional FA supplementation guidelines were more likely to be older, married and better educated (all $P < 0.05$). They were also less likely to have low income or to smoke, and were more likely to have used assisted reproduction and to have planned their pregnancy (all $P < 0.05$). The data also show that women who complied with the guideline to use FA >12 weeks preconceptionally were more likely to be older, married, nulliparous and well educated. They were also less likely to have low income or to smoke, and were more likely to have used assisted reproduction and to have planned their pregnancy (all $P < 0.05$).

Further comparisons were made adjusting for potential confounding factors using multivariate logistic regression analyses. When the binary logistic regression analysis was applied to assess the factors associated with preconceptional FA supplement use, only planning the pregnancy remained significant ($P < 0.001$) (Table 4). The full regression model from

Table 1 Characteristics of the study population

	(n = 587)
Age [years; mean (SD)]	30.5 (5.5)
Weight [kg; mean (SD)][a]	69.3 (15.4)
Body mass index [kg/m^2; mean (SD)][a]	25.8 (5.3)
Underweight [%; *n*]	1.9 (*n* = 11)
Normal weight [%; *n*]	50.7 (*n* = 296)
Overweight [%; *n*]	29.3 (*n* = 171)
Obese [%; *n*]	18.1 (*n* = 106)
Nulliparous [%; *n*][b]	40.2 (*n* = 235)
Marital status [%; *n*][b]	
Single	48.0 (*n* = 280)
Smoking [%; *n*][c]	
Current smoker	12.7 (*n* = 73)
Former smoker	35.2 (*n* = 203)
Never smoked	52.0 (*n* = 300)

[a]Data for $n = 584$.
[b]Data for $n = 583$.
[c]Data for $n = 576$.

Table 2 FA supplementation practices

	(n = 587)
Taking FA postconception	
Yes [%; *n*]	96.1 (564)
No [%; *n*]	3.9 (23)
Taking FA preconceptionally	
Yes [%; *n*]	42.9 (252)
No [%; *n*]	57.1 (335)
Taking FA >12 weeks preconceptionally	
Yes [%; *n*]	24.7 (145)
No [%; *n*]	75.3 (442)
Daily compliance in those taking FA[a]	
Yes [%; *n*]	97.7 (551)
No [%; *n*]	2.3 (13)

[a]Data for $n = 564$ who took FA during the pregnancy.

Table 3 Factors associated with FA supplement use by univariate analysis ($n = 587$)

	Taking FA before conception % (n)	*P*	*Taking FA for >12 weeks preconceptionally % (n)*	*P*
Body mass index (kg/m^2)				
<18.5 ($n = 11$)	36.4 (4)	0.240	18.2 (2)	0.915
18.5–24.9 ($n = 296$)	43.2 (128)		25.3 (75)	
25–29.9 ($n = 171$)	39.8 (68)		22.8 (39)	
30–34.9 ($n = 68$)	51.5 (35)		26.5 (18)	
35–39.9 ($n = 25$)	56.0 (14)		32.0 (8)	
≥40 ($n = 13$)	23.1 (2)		23.1 (3)	
Age (years)				
<22 ($n = 40$)	10 (4)	<0.001	0 (0)	<0.001
22–30 ($n = 247$)	34 (84)		19.8 (49)	
>30 ($n = 300$)	54.7 (164)		32 (96)	
Years living in Ireland				
<5 ($n = 28$)	46.4 (13)	0.908	17.9 (5)	0.505
5–10 ($n = 96$)	43.8 (42)		21.9 (21)	
>10 years ($n = 463$)	42.5 (197)		25.7 (119)	
Years of full-time education				
≤15 ($n = 107$)	31.8 (34)	<0.001	18.7 (20)	<0.001
16–18 ($n = 95$)	53.7 (51)		33.7 (32)	
>19 ($n = 60$)	66.7 (40)		45.0 (27)	
Age finished full-time education				
≤21 ($n = 146$)	38.4 (56)	<0.001	24.0 (35)	0.014
>22 ($n = 116$)	59.5 (69)		37.9 (44)	
Parity				
Nulliparous ($n = 235$)	45.5 (107)	0.307	30.2 (71)	0.011
Multiparous ($n = 349$)	41.3 (144)		20.9 (73)	
Planned pregnancy				
Yes ($n = 354$)	62.1 (220)	<0.001	36.2 (16)	<0.001
No ($n = 229$)	13.5 (31)		7.0 (16)	
Married				
Yes ($n = 296$)	56.8 (168)	<0.001	35.1 (104)	<0.001
No ($n = 287$)	28.9 (83)		13.9 (40)	
Current smoker				
No ($n = 503$)	46.5 (236)	<0.001	27.4 (137)	<0.001
Yes ($n = 73$)	17.8 (13)		6.8 (5)	
Place of birth				
Ireland ($n = 305$)	43.0 (187)	0.601	27.4 (118)	0.646
Outside Ireland ($n = 27$)	47.4 (18)		23.7 (9)	
Relative income poverty				
Yes ($n = 76$)	17 (13)	<0.001	7.9 (6)	<0.001
No ($n = 308$)	51 (157)		30.8 (95)	
Relative deprivation				
Yes ($n = 49$)	32.7 (16)	0.165	18.4 (9)	0.164
No ($n = 513$)	44.1 (226)		25.2 (130)	
Consistent poverty				
Yes ($n = 20$)	15 (3)	0.013	10.0 (2)	0.141
No ($n = 356$)	46.1 (164)		27.2 (97)	
Assisted reproduction				
Yes ($n = 12$)	91.7 (11)	0.004	75.0 (9)	<0.001
No ($n = 550$)	43.6 (240)		24.5 (135)	

Table 4 Multivariate analysis of factors associated with taking preconceptional FA[a]

		Taking FA >12 weeks preconceptionally			*Taking FA preconceptionally*		
		n	*Odds ratio (95% CI)*	P-*value*	n	*Odds ratio (95% CI)*	P-*value*
Age	Linear variable	174	1.025 (0.937–1.121)	0.589	174	1.045 (0.960–1.139)	0.311
Years of full-time education	≤15	68	1.0[b]		68	1.0[b]	
	16–18	66	1.172	0.724	66	1.165 (0.495–2.74)	0.727
	>19	40	1.495		40	1.625 (0.591–4.465)	
Smoking	Yes	18	0.655 (0.116–3.693)	0.632	18	0.511 (0.104–2.512)	0.409
	No	156	1.0[b]		156	1.0[b]	
Relative income poverty	Yes	33	0.792 (0.180–3.484)	0.758	33	0.539 (0.143–2.041)	0.363
	No	141	1.0[b]		141	1.0[b]	
Assisted reproduction	Yes	5	1.17 (0.49–2.83)	0.691	5	2.155 (0.229–20.30)	0.502
	No	169	1.0[b]		169	1.0[b]	
Married	Yes	92	1.98 (0.885–4.43)	0.096	92	1.31 (0.598–2.85)	0.503
	No	82	1.0[b]		82	1.0[b]	
Planned pregnancy	Yes	109	4.409 (1.1561–12.454)	0.005	109	8.66 (3.39–22.14)	<0.001
	No	65	1.0[b]		65	1.0[b]	
Parity	Nulliparous	65	2.58 (1.15–13.5)	0.021	65	2.019 (1.150–5.780)	0.100
	Multiparous	109	1.0[b]		109	1.0[b]	

CI, confidence interval; OR, odds ratio.

[a]Data for $n = 174$ for which all variables available.

[b]1.0 denotes the reference category.

which these data were derived explained 29.3% (Cox and Snell R^2e) to 39.1% (Nagelkerke R^2) of the variance in FA use preconceptionally.

When the binary logistic regression analysis was applied to assess the factors associated with FA supplementation for 12 weeks or more preconceptionally, only planning the pregnancy ($P = 0.005$) and nulliparous ($P = 0.021$) remained significant (Table 4). The full regression model from which these data were derived explained 18.0% (Cox and Snell R^2) to 25.3% (Nagelkerke R^2) of the variance in FA use for 12 weeks or more preconceptionally.

Discussion

Main findings of this study

This prospective observational study of women presenting for antenatal care found that only a quarter reported taking FA supplements optimally for >12 weeks before conception as recommended. Thus, three quarters of the women were at risk of having RCF levels low enough to increase their risk of having a baby with a NTD.[11,12] Only 5.7% ($n = 6$) of obese women took high-dose FA as recommended.

In the current study, univariate analysis showed that women who complied with periconceptional FA recommendations were more likely to be older, better educated, nulliparous and married. Women who complied were also less likely to be smokers or to have a low income, and were more likely to have planned their pregnancy (all $P < 0.05$). When multivariate analysis was performed, only planning the pregnancy persisted as a significant independent predictor of FA supplementation preconceptionally after adjustment for the other putative predictors (smoking, age, marriage, relative income poverty and years in full-time education). Also, only planning the pregnancy and nulliparous remained as independent predictors of preconceptional FA use for >12 weeks on multivariate binary logistic regression analysis.

What is already known on this topic?

Previous Irish studies have reported rates of FA use at any time during pregnancy from 84–88%.[21–23] These and other studies have also shown that 27–44% of women commence FA before conception.[21–24] Only one study commented on the duration of preconceptional FA intake.[21] This research showed that 36% of women take FA for >12 weeks preconceptionally which is consistent with our own findings. None of these studies have reported the dose of FA taken. To our knowledge, there is no data on the use of high-dose (5 mg) FA supplement use in obese women.

These findings highlight the need for improved public health messages about the benefits of preconceptional FA intake. There is also a need for consensus on periconceptional FA supplementation recommendations internationally as current guidelines vary considerably between countries, particularly regarding preconceptional FA use.

The factors found to be associated with preconceptional FA supplementation in the current study are consistent with those previously cited in the literature.[25–27] Existing Irish studies show that being married, older, a non-smoker and of lower parity are important predictors of FA supplementation in the preconceptional period, while lower socioeconomic status (in terms of income and educational attainment) predicts poorer preconceptional FA usage.[23,25–27]

In the current study, non-compliance with FA recommendations correlated with unfavourable socioeconomic characteristics such as low maternal education and relative income poverty, highlighting that socially disadvantaged women, the group at greatest risk of nutrient deficiency due to their poor diets, are the group least likely to take supplements.[28]

Previous studies have shown that planning a pregnancy is a consistent factor in predicting preconceptional FA use.[22,27] It is estimated that ~41% pregnancies are unplanned worldwide.[29] A recent Irish study examined recurrence of unplanned pregnancy.[30] It showed that of 3284 primigravidas who delivered in 2009, 1220 (37.1%) returned with a second pregnancy within 3 years of their first. The second pregnancy was unplanned in 248 (20.3%) women, and both pregnancies were unplanned in 124 (10.2%). Thus, the public health messages about FA supplementation need to emphasize that all women who could potentially become pregnant should take a FA supplement.

What this study adds

Unlike previous studies, we examined both the duration of preconceptional FA and the dosage of FA supplementation. Importantly, our study also examines compliance with recommended use of FA for ≥12 weeks preconceptionally which is the time taken to increase RCF to the level associated with a reduced risk of NTDs.[11]

Maternal obesity is associated with an increased risk of NTDs.[14] For this reason, in the UK, it is recommended that all women with a BMI of ≥30 kg/m^2 wishing to become pregnant should be advised to take 5 mg FA in the preconceptional period.[16] Irish guidelines also recommend high-dose supplementation in obesity.[15] No intervention or observational studies address prevention among other high-risk women.

In this study, uptake of high-dose FA supplementation guidelines in obesity was poor with only 5.7% of obese women taking high-dose FA, and only two of the women reporting obesity as being the sole reason for them taking high-dose FA.

To our knowledge, no studies have reported on the use of high-dose FA supplementation in obese women. This is prescient given the ongoing secular rise in the prevalence of obesity among 18–35 year old women in Ireland.[31] Obese women have been shown to be at higher risk of having a baby with a NTD.[32] Further research is needed to establish whether this high-dose FA recommendation for obese women is being implemented at a primary care level.

This study has strengths. Firstly, the information on FA supplementation was recorded using a structured questionnaire completed at a personal consultation with a single, trained dietetic researcher at the first antenatal visit. This reduced the risks of respondent error, recall bias or inter-observer variation. Unlike routine computerized records, the study recorded the timing and duration of FA supplementation which allowed us to collect in detail preconceptional FA supplement data, e.g. duration and dosage data that have not been done accurately to date. The supervised approach to data collection has been shown to result in lower levels of recall bias compared with self-administered questionnaires.[33]

Maternal socioeconomic, sociodemographic and anthropometric data, including measured weight, height and BMI, were also recorded accurately in a standardized way, further enhancing the integrity of these data.[34] Finally, the study sample is also representative of the broader national obstetric population from a socioeconomic and sociodemographic perspective, increasing the applicability and relevance of our findings in the public health context.

Limitations of this study

A potential weakness of the convenience sampling method employed in this study is that the findings may differ from the wider population in some unexpected ways (e.g., geographic area of residence). However, the hospital does accept women from all socioeconomic groups across the urban–rural divide. The hospital population has also become increasingly diverse as young people have become more mobile in Ireland and within the European Union. Self-selection bias is a further potential problem with convenience sampling, although again, our *post hoc* analyses have revealed our study population to be broadly representative of the wider population in terms of their major socioeconomic and sociodemographic characteristics. A challenge with all observational studies is the potential for confounding when evaluating the role of individual factors in predicating FA uptake. This, however, was addressed by using multivariate statistical analyses in examining our main outcomes of interest.

Conclusion

We recommend that the current FA recommendations for the prevention of NTDs are reviewed as a priority and communicated effectively by healthcare professionals and public health agencies, and that compliance with these guidelines among younger women needs to improve. At current dosages, women need to take FA for 12 weeks before conception and into the first trimester to achieve the RCF levels required to reduce the risk of NTD-affected births. All women who potentially could become pregnant, including those using selected forms of family planning, should be advised to take FA daily. Younger women of low socioeconomic status, those who smoke or who have already had children, and those who are not married should be targeted with health messages about the importance of FA supplementation. Obese women and their clinicians should also be made aware of the need to take high-dose FA for at least 12 weeks preconceptionally to ameliorate their higher risk of NTD-affected births.

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