

Do Italian pregnant women use periconceptional folate supplementation?

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Abstract

Introduction. Deficiency of folic acid (FA) has been identified as a risk factor for neural tube defects (NTDs) as well as other congenital anomalies. Thus, periconceptional folate supplementation is recommended for all women planning to get pregnant.

Methods. We conducted a KAP (knowledge, attitude, practice) survey to investigate the use of FA and its appropriateness. The survey included a sample of 562 women who delivered in the Lazio region between 2013 and 2014. Two logistic regression analyses were performed to evaluate the association between the characteristics of participating women and both the information received on FA intake and its use.

Results. The prevalence of periconceptional FA assumption was 19.4% although 82.2% of the interviewed women had planned their pregnancies.

Conclusions. It shows that more periconceptional counseling is needed to increase women's awareness on the opportunity of FA supplementation.

Key words

- folic acid
- pregnancy
- neural tube defects
- KAP survey

INTRODUCTION

Neural tube defects (NTDs) are severe congenital malformations with a prevalence between 0.2-10 cases per 1000 established pregnancies worldwide, thus ranking among the most common birth defects [1]. So far, in Italy, only regional data is available on NTD prevalence, namely from the registries of congenital anomalies of two regions: Emilia Romagna and Tuscany. In these regions, total birth prevalence of NTDs are 0.53 and 0.56 per 1000 respectively [2]. NTD are thought to arise during the third and fourth week after fertilization [3], the period of the most rapid growth of the fetus and highest requirement of FA. Many studies showed that FA deficiency is a risk factor for NTDs and other congenital anomalies when there is a predisposing genotype [4, 5]. Two randomized controlled trials [6, 7] on the efficacy of FA against NTDs have demonstrated that FA taken before pregnancy reduces the incidence of NTDs by 50-70% to a rate of approximately 0.6 per 1000 pregnancies. However, many women of childbearing age seem not to be aware of the preconceptional need of FA supplementation even in highly developed countries [8, 9]. Fortification of many cereal-grain foods became mandatory in the United States and in Canada already in 1998. This policy increased the average intake of FA among women of childbearing age by approximately 30 to 70% [10-12]. In Europe, national organizations have developed official guide-

lines [13]. The recommended approaches are different and include a number of strategies to reach red blood cell folate levels, providing the maximal protection from neural tube defects. The different recommendations depended on diet, ethnicity and genetic congenital anomaly risk status [14-16].

In 2004, the Italian Network for the promotion of FA intake [17] issued guidelines recommending FA supplementation for 4 weeks prior to conception and throughout the first trimester of pregnancy.

In order to investigate the prevalence of FA utilization and the information received on the proper periconceptional use of this vitamin, we conducted the present study analyzing data of a sample of women who delivered in three birth centers of the Italian National Health Service (NHS) in the Lazio region. Out of the 50 132 deliveries registered in the Lazio region in 2013, 98.4% took place in public birth centers [18], whereas around 80% of Italian women are assisted antenatally by a private gynecologist [19].

METHODS

In the present study, data were extrapolated from a multicenter survey aimed at investigating drug use during pregnancy [20]. The survey was conducted between 2013 and 2014 at three Italian birth centers within the Lazio region, one located in a big city and two in small towns, namely San Giovanni Calabita Fatebene Fratelli

Hospital (FBF) in Rome; Santa Maria Goretti Hospital (SMG) in Latina; and Belcolle Hospital in Viterbo. The target population were women of all ages, either Italian citizens or foreigners, who delivered in a defined study period set to analyze 200 consecutive births in each center. The eligibility criteria were absence of severe obstetric maternal complications and neonatal diseases and knowledge of Italian language. Women with chronic disease and/or NTDs risk factors were included. Representativeness of the sample has been investigated by comparing socio-demographic characteristics of the sample with those of women who delivered in 2013 in Italy [18]. Interviews were conducted by the use of a structured questionnaire, approved by the Italian National Institute of Health's ethical board. The questionnaire was administered by trained interviewers at the maternal and childcare unit of each hospital. The interviews were held in a special room to provide privacy, ensuring confidentiality and anonymity; the average time of questionnaire administration was 20 minutes. Each woman was asked to report about her socio-demographic profile and if pregnancy was planned. Information on the FA dose, modality and duration of treatment were collected. Out-of-pocket costs of FA treatment for women who planned pregnancy were estimated.

In order to investigate predictors of information received on the proper FA intake, a logistic regression analysis was performed. The following independent variables were used: age classes (≤ 29 , 30-34, ≥ 35); educational level (at least middle school graduation, high school graduation, university degree); profession (employed, unemployed or student, housewife), nationality (Italian, foreign), parity, planned pregnancy, previous adverse outcomes (spontaneous abortion, ectopic pregnancy or stillbirth) and birth center. In addition, to investigate on the proper FA use, a second logistic regression analysis on women who planned pregnancy was performed using the same predictors. Both of the analysis were adjusted for the type of antenatal care received during pregnancy (public or private).

Data were analyzed with the STATA/IC 11.0 version.

RESULTS

Overall, 562 women (93.7%) were interviewed, with 37 (6.2%) refusing to participate and one who could not be reached.

Socio-demographic characteristics and obstetric history

Characteristics of participants are shown in *Table 1*: the mean age was 31.9 years (range 17-48), 32.0% of the sample was older than 35 years. The majority of women were married or cohabitant (93.3%) and Italian (86.8%). Overall, among foreigners the largest group was from Romania (13.2%). Around half of the women were primiparous and had a high level of education: 81.6% had completed high school and among those 35.9% had a university degree. Almost 70% of the sample was employed, and 17.9% were housewives. Most women received antenatal care from a private gynecologist (80.2%) and 82.2% had planned their pregnancies.

Table 1

Socio-demographic characteristics and obstetric history of participating women (N = 562)

Characteristics		N	%
Age	≤ 29	183	32.9
	30-34	196	35.2
	≥ 35	178	32.0
Educational level	low	103	18.3
	medium	257	45.7
	high	202	35.9
Marital status	married/cohabitant	524	93.3
	employed	363	65.5
Employment	student/unemployed	92	16.6
	housewife	99	17.9
	Italian	488	86.8
Nationality	foreign	74	13.2
	primiparous	302	53.7
Parity	multiparous	260	46.3
	private Gynaecologist	425	80.2
Type of antenatal care	NHS Gynaecologist	73	13.8
	FHC	32	6.0
	Planned pregnancy	462	82.2
History of adverse obstetric outcomes*		100	17.8
Birth centre	Belcolle	195	34.7
	FBF	184	32.7
	SMG	183	32.6

*spontaneous abortion, ectopic pregnancy or stillbirth.

NHS = National Health Service.

FHC = Family Health Centres.

FBF = Fatebenefratelli Hospital.

SMG = Santa Maria Goretti Hospital.

Belcolle = Belcolle Hospital.

Type of information on FA received either before or during pregnancy

The percentage of interviewed women who received information on FA before or only during pregnancy was 42.0% and 46.3% respectively. *Table 2* describes in detail the information offered to the women. Almost all women received information from the gynecologist, 84.8% before and 97.6% during pregnancy. The General Practitioner (GP) informed only two women out of the total sample when none of women had been counseled by a midwife.

The logistic regression (*Table 3*) showed that graduated women were more likely to be informed on the use of FA (ORadj 2.11; CI 95% 1.12-3.95) together with those women who had planned their pregnancy (ORadj 2.90; CI 95% 1.65-5.10) and with those who had a history of previous adverse obstetric outcomes (ORadj 1.81; CI 95% 1.12-2.92). Women who delivered at Belcolle Hospital were more informed (49.7%) on the correct FA consumption when compared to women from SMG

Table 2

Information received on folic acid (FA) and periconceptual intake

	Before pregnancy		Only during pregnancy	
	N	%	N	%
Information received on FA	236	42.0	260	46.3
What is FA and its benefits	189	33.6	259	46.1
Recommended dosage	45	8.0	23	4.1
Recommended period of use	145	25.8	66	11.7
	All pregnancy		Planned pregnancy	
	N	%	N	%
Periconceptual FA intake	109	19.4	108	23.4

Table 3

Predictor variables associated with FA information received before pregnancy (N = 562) and logistic regression*

Variables	N	% FA informed	ORadj	CI 95%	
Interviewed women	562	42.0			
Age					
≤ 29	183	32.8	1		
30-34	196	43.9	1.22	0.74	2.00
≥ 35	178	49.4	1.40	0.85	2.31
Educational level					
low	103	32.0	1		
medium	257	36.6	1.12	0.65	1.94
high	202	54.0	2.11	1.12	3.95
Employment					
employed	363	48.2	1		
Student/ unemployed	92	28.3	0.64	0.36	1.12
housewife	99	29.3	0.57	0.32	1.02
Nationality					
Italian	488	45.9	1		
foreign	74	16.2	0.32	0.16	0.66
Parity					
primiparous	302	41.7	1		
multiparous	260	42.3	1.10	0.74	1.64
Planned pregnancy					
No	100	21.0	1		
Yes	462	46.5	2.90	1.65	5.10
History of adverse obstetric outcomes[§]					
No	462	40.0	1		
Yes	100	51.0	1.81	1.12	2.92
Birth centre					
Belcolle	195	49.7	1.00		
FBF	184	38.6	0.29	0.18	0.49
SMG	183	37.2	0.53	0.33	0.85

*adjusted for type of antenatal care received during pregnancy (public or private).

[§]spontaneous abortion, ectopic pregnancy or stillbirth.

FA = Folic Acid.

ORadj = adjusted Odds Ratio.

CI = Confidence Interval.

FBF = Fatebenefratelli Hospital.

SMG = Santa Maria Goretti Hospital.

Belcolle = Belcolle Hospital.

Table 4

Predictor variables associated with the recommended intake of FA in women who planned pregnancy (N = 462) and logistic regression*

Variables	N	% FA recommended	ORadj	CI 95%	
Women who planned pregnancy	462	23.4			
Age					
≤ 29	140	13.6	1		
30-34	163	29.5	2.00	1.03	3.88
≥ 35	155	25.8	1.63	0.83	3.19
Educational level					
low	75	9.3	1		
medium	207	19.8	2.02	0.78	5.27
high	179	34.1	3.44	1.27	9.27
Employment					
employed	314	29.0	1		
student/unemployed	78	9.0	0.73	0.33	1.61
housewife	62	14.5	0.39	0.16	0.96
Nationality					
Italian	413	25.2	1		
foreign	48	10.4	0.51	0.18	1.50
Parity					
primiparous	255	26.7	1		
multiparous	206	19.9	0.65	0.40	1.06
History of adverse obstetric outcomes[§]					
no	343	18.9	1		
yes	116	37.9	2.12	1.21	3.69
Birth centre					
Belcolle	156	25.0	1.00		
FBF	166	27.7	0.55	0.31	0.99
SMG	139	17.3	0.49	0.26	0.92

*adjusted for type of antenatal care received during pregnancy (public or private).

[§] spontaneous abortion, ectopic pregnancy or stillbirth.

FA = Folic Acid.

ORadj = adjusted Odds Ratio.

CI = Confidence Interval.

FBF = Fatebenefratelli Hospital.

SMG = Santa Maria Goretti Hospital.

Belcolle = Belcolle Hospital.

(OR 0.53; CI 95% 0.33-0.85) and from FBF (OR 0.29; CI 95% 0.18-0.49). Foreign women were less likely to be informed (adjusted OR 0.32, IC 95 % 0.16-0.66).

The prevalence of recommended use

Overall, the prevalence of recommended use of FA was 19.4%. The majority of interviewed women started FA treatment only during pregnancy (74.9%); 5.1% of women never used FA. The use of periconceptual FA between primiparous was higher than among multiparous (22.2% vs 16.2%). Recommended intake of FA was more common among women who planned pregnancies than between those with unplanned pregnancies (23.4% vs 1.0%).

Profile of women associated with the recommended intake of FA

Logistic regression analysis on data from women who planned pregnancies (N = 462; Table 4) showed that women aged 30-34 years were more likely to use periconceptual FA than those aged ≤ 29 (ORadj 2.00; CI 95% 1.03-3.88) as well as those with higher education compared with the less educated (ORadj 3.44; CI 95% 1.27-9.27). The probability to use FA properly was two times higher in women who had previous adverse pregnancy outcomes (ORadj 2.12; CI 95% 1.21-3.69) than those problem-free pregnancies. Also, women from FBF and SMG were less likely to use FA as recommended (ORadj 0.55 CI 95% 0.31-0.99; ORadj 0.49

CI 95% 0.26-0.92) compared with Belcolle Hospital. Finally, housewives were less likely to use FA with the recommended intake than employed women (adjusted ORadj 0.39; CI 95% 0.16-0.96).

Dosage and duration of FA treatment

The majority (76.0%) started the treatment only during the first trimester of pregnancy. Around 80% continued the treatment throughout pregnancy and only three women out of 562 assumed FA no longer than required (*i.e.*, first trimester). During pregnancy 47.2% took 0.4 mg per day and 45.4% more than 0.4 mg per day. In our sample none reported a previous NTD and the number of women with important risk factors for this condition is very low. Three women were in treatment with anti-epileptic drugs and 2 were affected by diabetes, all of them took 0.4 mg of FA.

Cost of FA treatment

The average out-of-pocket cost estimate of FA was 0.32 € per tablet. FA treatment costs were different depending on the duration and on the type of product. To calculate the average cost for each woman we divided women into two groups: 1) women who had taken FA antenatally and during pregnancy; 2) women who had taken FA only during pregnancy. Costs of FA treatment were on average 147 € (range 16-525 €) per group I and 106 € (range 15-441 €) per group II.

DISCUSSION

The present study provides an up-to-date insight on recommended FA intake among women giving birth in the Lazio region. We were interested in evaluating the women's awareness and actual use of FA. Although FA is obtainable free of charge through the NHS on prescription, this vitamin can also be purchased as an over-the-counter drug in Italy. The KAP survey was an essential tool in order to assess the actual consumption of FA because its use can only be partially electronically monitored.

Despite several initiatives that have been undertaken at national level [21, 22], preconceptional counseling offer is still low among health professionals. Only 42.0% of the interviewed women received proper counseling on FA preconceptional supplementation. Only 33.6% received antenatal information on its benefits and only 25.8% on the importance to take it at least one month before conception and in the first three months of pregnancy. A previous study performed in Italy [19] stressed the importance of family health centers (FHC) in periconceptional care and counselling. Since FHC are multidisciplinary/integrated services, they interact with young women on a regular or scheduled basis. These services might provide an ideal opportunity to share information regarding FA benefits. A survey conducted in Spain concluded that the information provided in primary care about periconceptional FA intake is crucial to promote its use during the protective period [9]. In our survey almost all women who had been informed received information from the gynecologist. This result is consistent with the fact that almost all Italian women are assisted antenatally by a

gynecologist [19]. Nevertheless GPs as well as midwives should be more involved in offering proactive preconceptional counseling on FA supplementation. We observed that women who delivered at Belcolle Hospital were more informed (49.7%) on the correct FA intake when compared to women from SMG and from FBF. Despite lack of information in order to detect the underlying reasons, this observation highlights an improvement opportunity.

Previous similar Italian surveys showed an increase in the intake of FA starting from 2004 when the national guidelines [17] were released and the Italian Network for the promotion of FA implemented its activities [23]. The FA periconceptional intake reached values between 21%-38% in the years 2008-2012 [19, 24-26]. Differences in rates observed in the mentioned studies were likely due to the different methodological approaches.

Although the preventive effect of FA has been demonstrated [6, 7], our study showed that these numbers did not improve further and highlighted that the recommended FA intake remained low (19.4%) even though 82.2% of participants planned their pregnancies. Well-educated women were more acknowledgeable on the necessity of FA intake. The higher educational degree of the interviewed women (35.9%) compared to those who delivered in Italy (25.9%) [18] could therefore only improve adherence to proper FA consumption.

This underlines the importance of providing appropriate counselling especially to women in disadvantaged socioeconomic conditions. Moreover, communication problems could partially explain why foreign women were less likely to take FA properly. Together, this information suggests that a more active role of health professionals is necessary in order to increase the overall FA use and to reduce social disparities.

Primiparous were more likely to take FA as compared with multiparous (22.2% vs 16.2%). Probably because the importance of appropriate FA intake was not explained by health professionals even before subsequent pregnancies. Alternatively, women with healthy children may have become less sensitive to the issue.

A considerable number of women (17.5%) had a longer and a higher FA intake than recommended (more than 0.4 mg per day) probably because only 8% received an appropriate counselling on FA dosage antenatally and 13.7% during pregnancy. Given the small number of women with risk factors for NTDs, we are confident that the proportion of women taking a high-dose of FA supplementation is not biased and that almost half of the sample took an inappropriate dosage of FA.

Other surveys implemented in Italy [19, 26] confirm the same risk factors detected in our study: multiparous, foreigners and less educated women are at higher risk of not taking FA as recommended. As reported in a French survey [27] also in the present study the likelihood of proper FA use was three times higher in women who had pregnancy complications in the past. Potentially health professionals were more prone to inform these patients. Alternatively, these women were more demanding in receiving advice or were more willing to follow preventative recommendations.

Finally, an estimate of the FA treatment cost per woman was calculated. Some women took the vitamin alone whereas others consumed it in combination with multivitamin supplements. Since these supplements are more expensive and not reimbursed by NHS, they constitute an extra cost. As additional vitamins provide no documented further benefit during uncomplicated pregnancy [28, 29] avoiding multivitamin supplements could be an opportunity to reduce out of pocket expenses. The cost of FA intake was also dependent on the duration of treatment and on the type of product with an estimate ranging from 16 € to 525 €. Since the Italian NHS covers the cost of the therapy, the price is not a true obstacle for the FA intake. However, women should also be informed of the gratuitousness of FA.

We conclude that more information and promotion of appropriate FA consumption from institutions and health professionals is required in order to inform women on the guidelines of FA intake and on its free availability. For this reason we setup a website offering several information regarding FA (www.epicentro.iss.it/temi/materno/consumo_farmaci_gravidanza/index.html).

Limitations of the present study include the region-specific nature of data. This factor limits the strength and the external validity of the conclusions of this study. Therefore, further studies involving women from a broader geographic distribution will help to provide more representative results.

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CONCLUSIONS

In Italy, the intake of periconceptional FA is incentivized: when prescribed, the expenses are reimbursed by the NHS. However, our survey shows that only 19.4% of women follow the FA periconceptional supplementation national guidelines. Young women, foreigners, housewives and women with lower educational level are less likely to take FA appropriately before and during pregnancy. Therefore, health providers and institutions are challenged to offer better counseling and information on FA periconceptional supplementation. FHCs, physicians (both gynecologists and GP) as well as midwives should have a greater proactive role in pre-conceptional counseling.

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Conflict of interest statement

The authors have no conflict of interest to declare.

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