



Folic acid supplementation use during the peri-conceptual period among professionals of a hospital in France

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ABSTRACT

Folic acid insufficiency is an important risk factor for congenital neural tube defects. Despite recommendations and national campaigns, the proportion of women taking folic acid in the peri-conceptual period remains insufficient worldwide. We describe in this study the proportion of peri-conceptual folic acid supplementation use and its determinants among a population of hospital workers during the course of a prevention campaign. We performed a single-center cross sectional study in a university hospital in France. Data were collected during 2 months in 2019 by an online questionnaire sent to all professionals. We collected information about folic acid supplementation use, its modalities (form, period, frequency and dosage) and reason for initiating or not supplementation. Response rate was 11.4 % (n = 1,075/9,447). Among the 748 women who reported at least one pregnancy, 72.7 % (95 % CI: 69.4–76.0 %) reported taking folic acid during their last pregnancy. Main reason for initiating supplementation was information given by a health professional (87.8 %), especially by gynaecologists-obstetricians. Principal factors associated with folic acid supplementation use were age between 25 and 35 years, high level of education and recent pregnancy. Folic acid supplementation use is still not systematic before and during pregnancy, even among health professionals. There is a case for mandatory folic acid fortification for the French general population.

1. Introduction

Neural tube defects (NTDs) which include spinal dysraphism (spina bifida) and anencephaly are the most common form of congenital anomalies of the central nervous system. From 2015 to 2020, the EUROCAT registry estimated the prevalence of spinal dysraphism in Europe at 1.65/10,000 live births and 4.19/10,000 pregnancies (i.e. live births, stillbirths and terminations of pregnancy) (European Commission, 2022). In France the prevalence of spinal dysraphism over the same period was 0.91/10,000 live births and 6.07/10,000 pregnancies (De la Fournière et al., 2020).

Spinal dysraphism and particularly myelomeningocele (i.e. open spina bifida) are in the vast majority of cases associated with motor and sensory impairment, lower urinary tract and anorectal disorders, sexual dysfunction and cognitive disorders; the most severe forms may lead to fetal death. There is no curative treatment and nearly ¾ of European couples choose to have a medical termination of pregnancy in case of

prenatal diagnosis (European Commission, 2022).

Folic acid insufficiency is an important risk factor for NTDs and is common during pregnancy because dietary intake is insufficient to cover daily needs, even with a balanced diet (ANSES, 2016; ANSES, 2021; Marchetta et al., 2015). Peri-conceptual folic acid supplementation use has been shown to reduce by 70 % the risk of NTDs and most health agencies in the United States and Europe recommend a supplementation of 400 µg/day oral folic during peri-conceptual period (Cawley et al., 2016; Toivonen et al., 2018; De-Regil et al., 2015; Viswanathan et al., 2017). However, despite these recommendations and national campaigns, the proportion of women taking folic acid in the peri-conceptual period remains insufficient and varies widely from one country to another from 32 to 51 % in North America and between 9 and 78 % in Europe (36 % in England, 45 % in Denmark, 19 % in Italy and 25 % in Spain) according to the pooled prevalence from studies published after 1990 (Toivonen et al., 2018). In France, the proportion of women who initiated supplementation of folic acid before pregnancy

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remains low although it has increased since the recommendations in 2009 (14.8 % in 2014, 23.2 % in 2016, and 28.3 % in 2021) (Le Ray et al., 2022). Possible factors associated with adequate supplementation of folic acid are higher socio-economic status, older maternal age, primiparity and planned pregnancy but results remain controversial (de Walle and de Jong-van den Berg LTW., 2008; Guillaume et al., 2020; Rousseau et al., 2021; Tort et al., 2013). Prevention campaigns in the general population also seem to have beneficial effect on folic acid intake in the peri-conceptional period (Ray et al., 2004).

This survey aimed to identify the proportion of peri-conceptional folic acid supplementation use and its determinants among a population of hospital workers during the course of a prevention campaign.

2. Methods

2.1. Design and study population

A descriptive single-center cross-sectional study was conducted by the spinal dysraphism reference center and the epidemiology and public health department of Rennes University Hospital over a week in September 2019. An online questionnaire published on the Sphinx Déclic platform was sent to all employees of Rennes University Hospital, health professionals or not, via their hospital e-mail address. A link was also posted on the institution's intranet in order to target professionals who did not have a hospital e-mail address. This survey amongst hospital workers was the first stage of a local campaign aimed to identify and understand the practices in folic acid intake in the peri-conceptional period and at the same time to raise the awareness of the need of folic acid supplementation use, since we added an information page at the end of the online survey. The campaign also included information stands organized in the hospital's convivial areas and information flyers distributed among professionals.

2.2. Collected data

The questionnaire collected information on the respondent's characteristics (age, gender, parity, occupation, level of education, and year of last pregnancy). Women who had had at least one pregnancy were asked about their own intake of folic acid supplementation before and/or during their last pregnancy. The different types of supplements were listed in the questionnaire. The reasons for initiating or not initiating supplementation were collected. Male professionals who reported a pregnancy of their partner were also asked to provide these data. If applicable, the supplementation modalities were detailed (form, frequency, dosage and period). The current recommendations in France suggest a supplementation of 400 µg per day to prevent dysraphism and 5 mg in case of NTDs antecedents whereas a dosage of 200 µg was initially recommended in the 1990 s French guidelines (Le Ray et al., 2022; Tort et al., 2013). Finally, professionals were asked about their knowledge of the benefits of the use of folic acid supplementation. All the data collected were anonymous. The study protocol was reviewed and approved by the ethics committee of Rennes University Hospital (approval No. 19.70).

2.3. Statistical analysis

Characteristics of study population were described overall and according to the respondent's gender, age, level of education, occupation and previous pregnancies. Prevalence of folic acid intake was estimated with a 95 % confidence interval. Reasons and modalities of folic acid intake were described, as well as the reasons for not taking folic acid.

Factors associated with folic acid supplementation use in women reporting at least one pregnancy were identified by bivariate and multivariate analysis using a logistic regression model. Variables introduced in the multivariate model were submitted to a backward selection. The professionals who answered "I don't know" to the question of

folic acid supplementation use during their last pregnancy were initially excluded from the analysis. A sensitivity analysis was conducted considering that they had not taken any supplementation. The level of significance was 0.05. Analyses were performed using SAS 9.4 software.

3. Results

The participation rate was 11.4 % (1,075/9,447 employees of Rennes university hospital during the study period, Fig. S1). The majority of respondents were women (87.3 %), aged between 30 and 40 years (39.2 %) and most often technical and administrative staff or nurses and health managers (respectively 33.5 % and 28.0 %) (Table 1).

Among the 748 women who had had at least one pregnancy, 68.9 % (95 %CI: 65.5–72.2 %) reported the use of folic acid supplementation before and/or during their last pregnancy, 25.8 % reported no use of folic acid supplementation, and 5.3 % did not know (Table 2). Among the 91 men whose partner had experienced at least one pregnancy, 62.6 % reported that their partner had taken folic acid, 17.6 % that she had not, and 19.8 % did not know.

Table 1

Demographic and social characteristics of the professionals who responded to the online questionnaire on peri-conceptional use of folic acid (n = 1075), Rennes, France, 2019.

| | Women (n = 938) n (%) | Men (n = 137) n (%) | All (n = 1,075) n (%) |
|--|--------------------------|------------------------|--------------------------|
| Age at the day of the survey (years) | | | |
| <30 | 153 (16.3) | 24 (17.5) | 177 (16.5) |
| 30–40 | 361 (38.5) | 60 (43.8) | 421 (39.2) |
| 40–50 | 244 (26.0) | 31 (22.6) | 275 (25.6) |
| ≥50 | 180 (19.2) | 22 (16.1) | 202 (18.8) |
| Number of previous pregnancy(ies) | | | |
| 0 | 190 (20.3) | 46 (33.6) | 236 (21.9) |
| 1 | 193 (20.6) | 24 (17.5) | 217 (20.2) |
| 2 | 349 (37.2) | 45 (32.8) | 394 (36.6) |
| ≥3 | 206 (21.9) | 22 (16.1) | 228 (21.2) |
| Time since the last pregnancy (years)^a | | | |
| ≤10 | 462 (61.8) | 62 (68.1) | 524 (62.5) |
| 10–20 | 194 (25.9) | 17 (18.7) | 211 (25.1) |
| >20 | 92 (12.3) | 12 (13.2) | 104 (12.4) |
| Age at the last pregnancy^a | | | |
| ≤25 y | 33 (4.4) | – | – |
| 25–35 y | 534 (71.4) | – | – |
| ≥35 y | 181 (24.2) | – | – |
| Level of education | | | |
| Primary or secondary school | 43 (4.6) | 3 (2.2) | 46 (4.3) |
| High school diploma (baccalauréat) | 103 (11.0) | 10 (7.3) | 113 (10.5) |
| 2 years after diploma | 191 (20.4) | 10 (7.3) | 201 (18.7) |
| 3–4 years after diploma | 313 (33.4) | 29 (21.2) | 342 (31.8) |
| ≥5 years after diploma | 288 (30.7) | 85 (62.0) | 373 (34.7) |
| Occupation | | | |
| Nursing assistant | 73 (7.8) | 2 (1.5) | 75 (7.0) |
| Nurse or nurse manager | 276 (29.4) | 25 (18.2) | 301 (28.0) |
| Midwife | 31 (3.3) | 2 (1.5) | 33 (3.0) |
| Physician (including junior) | 109 (11.6) | 49 (35.8) | 158 (14.7) |
| Gynaecologist-Obstetrician | 10 (0.9) | 0 (0.0) | 10 (6.3) |
| General practitioner | 8 (7.3) | 4 (8.2) | 12 (7.6) |
| Pediatrician | 14 (12.8) | 2 (4.1) | 16 (10.1) |
| Other medical specialties | 61 (56.0) | 33 (67.3) | 94 (59.5) |
| Other surgical specialties | 9 (8.2) | 5 (10.2) | 14 (8.9) |
| Unknown | 7 (6.4) | 5 (10.2) | 12 (7.6) |
| Pharmacist | 17 (1.8) | 6 (4.4) | 23 (2.1) |
| Other healthcare professionals ^b | 109 (11.6) | 16 (11.7) | 125 (11.6) |
| Technical or administrative staff | 323 (34.4) | 37 (27.0) | 360 (33.5) |

^a Among 748 women reported at least one pregnancy.

^b Radio manipulator, laboratory technician, physiotherapist, occupational therapist, dietician, psychologist, genetic counsellor, pharmacy technician, hospital porter.

Table 2

Description of folic acid supplementation use, reasons and modalities of supplementation among hospital professionals reporting at least one pregnancy (n = 839), Rennes, France, 2019.

| | Women (n = 748) n (%) ^a | Men (n = 91) n (%) ^a |
|---|---------------------------------------|------------------------------------|
| Folic acid supplementation use before and/or during the last pregnancy | | |
| Yes | 515 (68.9) | 57 (62.6) |
| No | 193 (25.8) | 16 (17.6) |
| Do not know | 40 (5.3) | 18 (19.8) |
| Discussion with a health professional before starting the pregnancy | | |
| Yes | 292 (52.6) | 34 (45.3) |
| No | 255 (45.9) | 37 (49.3) |
| Do not know | 8 (1.4) | 4 (5.3) |
| Reason for initiating supplementation ^{b, c} | | |
| Information given by a health professional | 452 (87.8) | 43 (75.4) |
| General practitioner | 78 (15.1) | 10 (17.5) |
| Obstetrician gynecologist | 297 (57.7) | 29 (50.9) |
| Midwife | 52 (10.1) | 2 (3.5) |
| Pharmacist | 0 (0.0) | 0 (0.0) |
| Nurse | 1 (0.2) | 0 (0.0) |
| Unspecified | 24 (4.7) | 2 (3.5) |
| Learned through studies | 83 (16.1) | 20 (35.1) |
| Heard about it in the media | 13 (2.5) | 0 (0.0) |
| Someone I know told me about it | 24 (4.7) | 3 (5.3) |
| Took a supplement without knowing it contained folic acid | 7 (1.4) | 5 (8.8) |
| Do not know | 7 (1.4) | 0 (0.0) |
| Form ^c | | |
| Folic acid only | 308 (62.9) | |
| Folic acid in multivitamin supplement | 162 (33.1) | |
| Do not know | 20 (4.1) | |
| Frequency ^c | | |
| Every day | 421 (81.7) | |
| Every 2 days | 7 (1.4) | |
| Less than 1 day/2 | 10 (1.9) | |
| Do not know | 77 (14.9) | |
| Dosage ^c | | |
| 200 µg | 12 (2.4) | |
| 400 µg | 80 (15.7) | |
| 5 mg | 42 (8.2) | |
| Do not know | 375 (73.7) | |
| Period of supplementation ^c | | |
| Before pregnancy | | |
| Yes | 243 (83.2) | |
| No | 38 (13.0) | |
| Do not know | 11 (3.8) | |
| During pregnancy | | |
| Yes | 252 (87.2) | |
| No | 18 (6.2) | |
| Do not know | 19 (6.6) | |
| Reason for not taking supplementation ^{b,d} | | |
| No information given | 170 (88.1) | |
| Unplanned pregnancy | 11 (5.7) | |
| Did not want to take supplementation | 9 (4.7) | |
| Prescribed but forgot to take it | 3 (1.5) | |
| Unspecified | 1 (0.5) | |
| Missing data: discussion with a health professional before starting the pregnancy (n = 193 for women and n = 16 for men); form (n = 25); dosage (n = 6); period of supplementation before pregnancy (n = 223), after pregnancy (n = 226); Reason for not taking supplementation (n = 1 for women and n = for men) | | |
| ^a Percentages are calculated on available data (excluding missing data) | | |
| ^b Several answers possible | | |
| ^c Among professionals who declared folic acid supplementation use (women n = 515, men n = 57) | | |
| ^d Among professionals who declared no folic acid supplementation use (n = 193) | | |

Folic acid supplementation use was motivated in the majority of cases by information provided by an obstetrician-gynecologist, more rarely by a general practitioner or a midwife. Folic acid was most often taken alone (and not with other dietary supplements) and nearly 3/4 of the women declared having taken a supplement both before and after the beginning of the pregnancy.

Of the 193 women who reported not having taken folic acid before or during their last pregnancy, 88.1 % (n = 170) declared that they had not been given the information (including two employees who said they had been given the information but late in the pregnancy), in 5.7 % (n = 11) the pregnancy was unplanned. Only 4.7 % (n = 9) did not want to take it and 1.5 % (n = 3) indicated that they had been prescribed folic acid but had forgotten to take it. Among the women who indicated that they did not wish to take supplements, three employees thought that a balanced diet was sufficient for folic acid intake: "I did not want to over-medicate my pregnancy at the time, thinking that eating well would be enough", "Sufficient food intake", "Balanced diet without the need for supplements".

Women's age at last pregnancy (p = 0.049), level of education (p = 0.041), and time since the last pregnancy (p < 0.001) were factors significantly associated with the use of folic acid supplementation in multivariate analysis (Table 3). Similar results were found in the sensitivity analysis.

In addition, the rate of employees declaring that they knew why it was recommended to take folic acid before and during pregnancy was 61.2 % (n = 656) overall, 62.5 % of women (n = 584) and 52.9 % of men (n = 72), 92.4 % of doctors (n = 145), 97.0 % of midwives (n = 32), 62.2 % of nurses and health care managers (n = 186), 40.0 % of health care assistants (n = 30), and 45.1 % of the technical or administrative staff (n = 162). The explanations given by the professionals spontaneously mentioned the term "spina bifida" in 24.7 % of cases (n = 162) and the term neural tube in 22.9 % of cases (n = 150).

Finally, 31.7 % of the women surveyed (n = 308) reported having already advised a woman wishing to start a pregnancy to take folic acid.

4. Discussion

4.1. Principal findings

Nearly 70 % of the women (respondent or partner of respondent) reported having taken folic acid supplements before and/or during pregnancy. The factors associated with folic acid supplementation use were age of women at the last pregnancy, their education level and the time since the last pregnancy.

4.2. Interpretation

4.2.1. Proportion of folic acid supplementation

The prevalence of folic acid supplementation use in the periconceptional period was significantly higher than in studies already published in France (14.8 to 36.3 %) (Le Ray et al., 2022; Guillaume et al., 2020; Tort et al., 2013). This is probably explained by our specific sample made up of hospital workers, 2/3 of whom were health professionals who acquired specific knowledge during their studies.

4.2.2. Factors associated with inadequate supplementation

Consistent with previous studies, our results showed that younger women were less likely to use folic acid supplementation compared to women aged between 25 and 35 and women with higher education are more likely to use it compared with women who had studied up to primary or secondary school (Rousseau et al., 2021; Tort et al., 2013; Wegner et al., 2020; Bestwick et al., 2014). These factors reflect social inequalities in prevention that could be explained by lower access to care and reception of prevention campaigns, lower concern and knowledge about women's health or more unplanned pregnancies (Lindquist et al., 2015). Financial reasons could also be mentioned as an obstacle but this seems unlikely in France as folic acid supplements are free if prescribed by a medical professional and the cost of folic acid supplementation bought over the counter is less than 3€/month (OECD, 2021). Our results also indicate that women whose last pregnancy was ≤10 years ago were more likely to have taken folic acid supplementation than women reporting a last pregnancy more than 10 years ago.

Table 3

Factors associated with the use of folic acid supplementation among women reporting at least one pregnancy and having taken or not folic acid supplementation (excluding “I don’t remember”) (n = 708), Rennes, France, 2019.

| | Folic acid supplementation use (n = 515) | No folic acid supplementation use (n = 193) | Crude OR [95 %CI] | P | Adjusted OR ^b [95 %CI] | P |
|--|--|---|--------------------|--------|-----------------------------------|--------|
| Age at the last pregnancy, year | | | | 0.041 | | 0.049 |
| ≤ 25 | 16 (3.1) | 13 (6.7) | 0.41 [0.19–0.88] | | 0.47 [0.18–1.19] | |
| 25–35 | 381 (74.0) | 128 (66.3) | Ref. | | Ref. | |
| ≥ 35 | 118 (22.9) | 52 (26.9) | 0.76 [0.52–1.12] | | 0.63 [0.41–0.98] | |
| Level of education | | | | <0.001 | | 0.041 |
| Primary or secondary school | 12 (2.3) | 19 (9.8) | Ref. | | Ref. | |
| High school diploma (baccalaureat) | 47 (9.1) | 21 (10.9) | 3.54 [1.46–8.6] | | 3.42 [1.21–9.66] | |
| 2 years after diploma | 110 (21.4) | 39 (20.2) | 4.47 [1.99–10.04] | | 3.97 [1.53–10.28] | |
| 3–4 years after diploma | 179 (34.8) | 73 (37.8) | 3.88 [1.79–8.40] | | 3.61 [1.44–9.03] | |
| ≥ 5 years after diploma | 167 (32.4) | 41 (21.2) | 6.45 [2.90–14.34] | | 4.45 [1.74–11.37] | |
| Occupation | | | | 0.014 | | |
| Nurse or nurse management | 159 (30.9) | 71 (36.8) | 0.76 [0.51–1.14] | | | |
| Physician, midwife or pharmacist | 86 (16.7) | 17 (8.8) | 1.71 [0.94–3.11] | | | |
| Nursing assistant | 30 (5.8) | 21 (10.9) | 0.48 [0.26–0.91] | | – | – |
| Other healthcare professionals ^a | 60 (11.6) | 23 (11.9) | 0.88 [0.50–1.55] | | | |
| Technical or administrative staff | 180 (34.9) | 61 (31.6) | Ref. | | | |
| Number of previous pregnancy | | | | <0.001 | | |
| 1 | 155 (30.1) | 30 (15.5) | Ref. | | | |
| 2 | 227 (44.1) | 101 (52.3) | 0.43 [0.28–0.69] | | – | – |
| ≥ 3 | 133 (25.8) | 62 (32.1) | 0.41 [0.25–0.68] | | | |
| Time since the last pregnancy (years) | | | | <0.001 | | <0.001 |
| ≤ 10 | 393 (76.3) | 30.0) | 14.63 [8.46–25.32] | | 14.11 [7.99–24.92] | |
| 10–20 | 97 (18.8) | 81 (42.0) | 2.59 [1.48–4.52] | | 2.46 [1.37–4.43] | |
| > 20 | 25 (4.8) | 54 (28.0) | Ref. | | Ref. | |

OR: Odds Ratio, CI: Confidence Interval.

^a radio manipulator, laboratory technician, physiotherapist, occupational therapist, dietician, psychologist, genetic counsellor, pharmacy technician, hospital porter.

^b OR adjusted on variables selected from backward procedure in the logistic regression model.

This probably reflects the dissemination of supplementation recommendations to the general public in France in the late 2000s (Haute Autorité de Santé, 2009).

4.2.3. Importance of information and prescription by health professionals

Lack of information on the benefit of folic acid was the first reason mentioned by women who reported no folic acid supplementation use during their last pregnancy. A first hypothesis to explain this lack of information could be a lack of appropriation of the recommendations by health professionals likely to be in contact with women before and during pregnancy, i.e. obstetrician-gynaecologists, general practitioners or sometimes midwives (Bitzer et al., 2013). However, in our sample, almost all physicians and midwives stated that they were aware of the usefulness of supplementation and were familiar with the prescription procedure.

Another issue is the difficulty to reach women before the beginning of their pregnancy to deliver this information. In our sample, only half of the women mentioned their pregnancy intention to a health professional; this is consistent with a European survey which found that nearly 60 % of women indicated that they had stopped using their method of contraception without first consulting a health care professional (Bitzer et al., 2013). Similarly, a recent French population-based study has estimated that only 37.9 % of women consulted a health professional in anticipation of a pregnancy, in spite of a pre-conception consultation having been recommended by French health authorities since 2009 (Haute Autorité de Santé, 2009; Enquête nationale périnatale - Rapport, 2021). In France, a recent health regulation introduced a medical consultation at each key age of life, including a consultation between the ages of 20 and 25, which could be a time to deliver this information (Loi de Financement de la Sécurité Sociale, 2023).

The role of community pharmacists for counselling women of childbearing age about folic acid intake is also currently discussed

(Prabahar and Alenazi, 2020), however, ours results as well as previous studies indicated that information is still rarely delivered in this context (Prabahar and Alenazi, 2020; Rodrigues and Dipietro, 2012). This could be explained by the difficulty of raising the subject with a woman of childbearing age who is consulting for another reason.

Moreover, if the information is delivered at the right time, i.e. in the pre-conceptional period, the question is to know how it is delivered and what impact this information may have on the woman’s behaviour with regard to taking folic acid supplementation. In the Guillaume et al. study, only a quarter of the women had a correct perception of the reason for the use of folic acid supplementation, 16.1 % of them justified non-adherence to supplementation by a lack of understanding of the reason for supplementation and a third declared that they had not retained any information on the folic acid supplementation that had been prescribed (Guillaume et al., 2020). Finally, a large survey among 22,925 European women reported that only 17 % of women were aware that folic acid reduces the risk of NTDs (Bitzer, 2013).

4.2.4. Collective information through prevention campaigns

Mass prevention campaigns in the general population have been also recognized as useful tools to inform couples and healthcare professionals and improve the folic acid intake in the peri-conceptional period. Thus, in the review of Ray et al, mass media campaigns on peri-conceptional use of folic acid increased significantly the rate of folic acid supplementation intake by a factor of 1.7 to 7.2, but the post-campaign rate never reached 50 % (Ray et al., 2004). These campaigns allow the general population to be reached and not just women of reproductive age. However, one of the main limitations is that they may increase social inequalities in health (Amitai et al., 2004).

Nevertheless, it remains difficult to spread a message of prevention concerning a rare and potentially serious pathology to women who do not necessarily have a pregnancy plan. Moreover, when there is a

pregnancy plan, it implies taking a daily medication, in healthy women, sometimes for many months in case of fertility disorders.

4.2.5. Mandatory folic acid fortification

These reasons explain why, despite recommendations and successive prevention campaigns, the rate of supplementation use remains insufficient in Europe particularly among the most disadvantaged mothers (Toivonen et al., 2018; Le Ray et al., 2022; Haggarty, 2021). Over 60 countries in America, Africa and Asia have decided to introduce mandatory folic acid fortification in wheat flour, maize flour and rice kernels (Kancherla et al., 2022). Although there is evidence that such strategy is effective, safe, socially equitable and cost-effective in reducing the prevalence and severity of NTDs it has not yet been introduced in Europe, except in Kosovo. The United Kingdom plans however to mandate folic acid fortification in wheat flour and this decision should become effective by 2024 (Rodrigues and Dipietro, 2012; Haggarty, 2021; Kancherla et al., 2022; Williams et al., 2015; Mai et al., 2022; Irvine et al., 2015; Atta et al., 2016; Pardo et al., 2022; Global Fortification Data Exchange, 2023). The number of NTD potentially prevented by flour fortification has been estimated up to 1,000 NTDs per year in Europe (Honein et al., 2001; Morris et al., 2021). Several recent positions of researchers including the European Board and College of obstetrics and gynaecology have called for mandatory flour fortification with folic acid (Kancherla et al., 2022; Kancherla et al., 2022; Wald, 2022; Kar et al., 2022; Petch et al., 2022; Smith et al., 2022).

5. Strengths and limitations

To our knowledge, this study is the first one carried out in France over the last ten years on a sample of this size including both women and men. This study allowed to assess the knowledge of a large sample of hospital workers in a French University Hospital about the benefit of folic acid intake in peri-conceptional period. The survey was in itself a means of raising awareness of the recommendations concerning the use of folic acid supplementation among all hospital workers whether healthcare professionals or not. However, several limitations can be raised. Our sample consists of hospital workers and the results are not necessarily representative of the general population. There is an obvious selection bias as only 11.4 % of hospital employees answered our survey and the responders were more likely to be more attentive to this health issue. The medical professions were over-represented compared to the paramedical and administrative professions since the participation in this survey was on a voluntary basis and required having an individual professional email address, which is not the case for many paramedical employees. Moreover, some hospital workers may have exchanged views on the subject during the survey period, this may have influenced the results. In addition, the data collected concerning the use of folic acid supplementation were only declarative and could have been affected by memory bias if the last pregnancy had taken place in the distant past and by social desirability for health professionals. The number of men who responded to the questionnaire is limited, but data concerning them are still scarce (Yargawa and Leonardi-Bee, 2015). However, their role in pregnancy-related prevention as recipients of prevention messages, whether individually via health professionals or collectively via information campaigns, appears essential to increase the rate of intake of folic acid supplementation in the peri-conceptional period.

6. Conclusion

Folic acid supplementation use is still not systematic in before and during pregnancy, even among health professionals, who are supposed to be more aware of its benefits than the general population. Individual information for women and couples planning a pregnancy, and regular information campaigns run by the health authorities, have so far failed to provide a totally satisfactory response in France. There is certainly a

case for mandatory folic acid fortification for the French general population.

CRedit authorship contribution statement

Pauline Blanc-Petitjean: Writing – original draft, Validation. **Magali Jézequel:** Validation, Conceptualization. **Andrea Manunta:** Validation. **Camille Olivari-Philipponnet:** Conceptualization. **Emmanuelle Samson:** Validation. **Emma Bajeux:** Writing – review & editing, Writing – original draft, Validation, Supervision, Methodology, Formal analysis.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request.

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Appendix A. Supplementary data

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References

- Amitai, Y., Fisher, N., Haringman, M., Meiraz, H., Baram, N., Leventhal, A., 2004. Increased awareness, knowledge and utilization of preconceptional folic acid in Israel following a national campaign. *Prev. Med.* 39 (4), 731–737.
- ANSES, 2016. Données de consommations et habitudes alimentaires de l'étude INCA 2, France [Internet]. 2016 [cited 2022 Dec 1]. Available from: <https://www.data.gouv.fr/fr/datasets/donnees-de-consommations-et-habitudes-alimentaires-de-letude-inca-2-3/>.
- ANSES, 2021. Les références nutritionnelles en vitamines et minéraux Connaître, évaluer, protéger Avis de l'Anses Rapport d'expertise collective [Internet]. 2021 Mar. Available from: <https://www.anses.fr/fr/system/files/NUT2018SA0238Ra.pdf>.
- Atta, C.A.M., Fiest, K.M., Frolkis, A.D., Jette, N., Pringsheim, T., St Germaine-Smith, C., et al., 2016. Global birth prevalence of spina bifida by folic acid fortification status: a systematic review and meta-analysis. *Am. J. Public Health* 106 (1), e24–e34.
- Bestwick, J.P., Huttly, W.J., Morris, J.K., Wald, N.J., 2014. Prevention of Neural Tube Defects: A Cross-Sectional Study of the Uptake of Folic Acid Supplementation in Nearly Half a Million Women. Rosenfeld CS, editor. *PLoS ONE*. ;9(2):e89354.
- Bitzer, J., von Stenglin, A., Bannemerschult, R., 2013. Women's awareness and periconceptional use of folic acid: data from a large European survey. *Int. J. Womens Health* 5, 201–213.
- Bitzer J, von Stenglin, 2013. Bannemerschult. Women's awareness and periconceptional use of folic acid: data from a large European survey. *IJWH*. 201.
- Cawley, S., Mullaney, L., McKeating, A., Farren, M., McCartney, D., Turner, M.J., 2016. A review of European guidelines on periconceptional folic acid supplementation. *Eur. J. Clin. Nutr.* 70 (2), 143–154.
- De la Fournière, B., Dhombres, F., Maurice, P., De Foucaud, S., Lallemand, P., Zerah, M., et al., 2020. Prevention of neural tube defects by folic acid supplementation: a national population-based study. *Nutrients* 12 (10), 3170.
- de Walle, H.E.K., de Jong-van den Berg LTW., 2008. Ten years after the Dutch public health campaign on folic acid: the continuing challenge. *Eur. J. Clin. Pharmacol.* 64 (5), 539–543.
- De-Regil, L.M., Peña-Rosas, J.P., Fernández-Gaxiola, A.C., Rayco-Solon, P., 2015. Effects and safety of periconceptional oral folate supplementation for preventing birth defects. *Cochrane Database Syst. Rev.* 14 (12). CD007950.
- Enquête nationale périnatale - Rapport 2021. [Internet]. 20Available from: <https://www.santepubliquefrance.fr/content/download/474395/3629352?version=4>.

- European Commission, 2022. EU Science Hub, European Platform on Rare disease Restriction, EUROCAT, DATA, EUROCAT. Prevalence per 10,000 Births. Neural Tube Defects, 2015 to 2020. All Full Registries. [Internet]. [cited 2022 Dec 1]. Available from: https://eu-rd-platform.jrc.ec.europa.eu/eurocat/eurocat-data/prevalence_en.
- Global Fortification Data Exchange | GFDx – Providing actionable food fortification data all in one place. [Internet]. [cited 2023 Nov 22]. Available from: <https://fortificationdata.org/>.
- Guillaume, M., Riquet, S., Zakarian, C., Comte, F., 2020. Supplémentations en fer, acide folique, vitamine D pendant la grossesse : observance des patientes. *Santé Publique*. 32 (2), 161.
- Haggarty, P., 2021. UK introduces folic acid fortification of flour to prevent neural tube defects. *Lancet*. 398 (10307), 1199–1201.
- Haute Autorité de Santé, 2009. Projet de grossesse : informations, messages de prévention, examens à proposer [Internet]. p. 2009. Available from: https://www.has-sante.fr/upload/docs/application/pdf/2010-01/projet_de_grossesse_informations_messages_de_prevention_examens_a_proposer_argumentaire.pdf.
- Honein, M.A., Paulozzi, L.J., Mathews, T.J., Erickson, J.D., Wong, L.Y., 2001. Impact of folic acid fortification of the US food supply on the occurrence of neural tube defects. *JAMA*. 285 (23), 2981–2986.
- Irvine, B., Luo, W., León, J., 2015. Report Summary - Congenital Anomalies in Canada 2013: A Perinatal Health Surveillance Report by the Public Health Agency of Canada's Canadian Perinatal Surveillance System. *Health Promot. Chronic Dis. Prev. Can.* 35 (1), 21–22.
- Kancherla, V., Wagh, K., Priyadarshini, P., Pachón, H., Oakley, G.P., 2022. A global update on the status of prevention of folic acid-preventable spina bifida and anencephaly in year 2020: 30-Year anniversary of gaining knowledge about folic acid's prevention potential for neural tube defects. *Birth Defects Res.* 114 (20), 1392–1403.
- Kancherla, V., Botto, L.D., Rowe, L.A., Shlobin, N.A., Caceres, A., Arynchyna-Smith, A., et al., 2022. Preventing birth defects, saving lives, and promoting health equity: an urgent call to action for universal mandatory food fortification with folic acid. *Lancet Global Health* 10 (7), e1053–e1057.
- Kar, A., Yajnik, C.S., Doke, P.P., Bhide, P., Chutke, A., Radhakrishnan, B., et al., 2022. Mandatory food fortification with folic acid. *Lancet Global Health* 10 (10), e1390.
- Le Ray C, Lelong N, Cinelli H, Blondel B, 2022. Results of the 2021 French National Perinatal Survey and trends in perinatal health in metropolitan France since 1995. *J. Gynecol. Obstetrics Human Reproduct.* [Internet]. 2022 Dec [cited 2022 Dec 1];51 (10). Available from: <https://pubmed.ncbi.nlm.nih.gov/36410664/>.
- Lindquist, A., Kurinczuk, J.J., Redshaw, M., Knight, M., 2015. Experiences, utilisation and outcomes of maternity care in England among women from different socio-economic groups: findings from the 2010 National Maternity Survey. *BJOG*. 122 (12), 1610–1617.
- Loi de Financement de la Sécurité Sociale 2023 [Internet]. Available from: <https://www.legifrance.gouv.fr/eli/loi/2022/12/23/ECOX2225094L/jo/texte>.
- Mai, C.T., Evans, J., Alverson, C.J., Yue, X., Flood, T., Arnold, K., et al., 2022. Changes in Spina Bifida Lesion Level after Folic Acid Fortification in the US. *J. Pediatrics* 249, 59–66.e1.
- Marchetta, C.M., Devine, O.J., Crider, K.S., Tsang, B.L., Cordero, A.M., Qi, Y.P., et al., 2015. Assessing the association between natural food folate intake and blood folate concentrations: a systematic review and Bayesian meta-analysis of trials and observational studies. *Nutrients* 7 (4), 2663–2686.
- Morris, J.K., Addor, M.C., Ballardini, E., Barisic, I., Barrachina-Bonet, L., Braz, P., et al., 2021. Prevention of neural tube defects in Europe: a public health failure. *Front. Pediatr.* 24 (9), 647038.
- OECD, 2021. Health at a Glance 2021: OECD Indicators [Internet]. OECD; 2021 [cited 2023 Mar 8]. (Health at a Glance). Available from: https://www.oecd-ilibrary.org/social-issues-migration-health/health-at-a-glance-2021_ae3016b9-en.
- Pardo, R., Vilca, M., Villaruel, L., Davalji, T., Obrycki, J.F., Mazumdar, M., et al., 2022. Neural tube defects prevalence does not increase after modification of the folic acid fortification program in Chile. *Birth Defects Res.* 114 (7), 259–266.
- Petch, S., McAuliffe, F., O'Reilly, S., Murphy, C., Coulter-Smith, S., de Campos, D.A., et al., 2022. Folic acid fortification of flour to prevent neural tube defects in Europe – A position statement by the European Board and college of obstetrics and gynaecology (EBCOG). *Eur. J. Obstetrics Gynecol. Reproductive Biol.* 279, 109–111.
- Prabakar, K., Alenazi, T., 2020. Role of pharmacist's counseling on folate compliance. *Saudi J. Health Sci.* 9 (3), 221.
- Ray, J.G., Singh, G., Burrows, R.F., 2004. Evidence for suboptimal use of periconceptional folic acid supplements globally. *BJOG: Int. J. Obs. Gyn.* 111 (5), 399–408.
- Rodrigues, C.R., Dipietro, N.A., 2012. Knowledge of folic acid and counseling practices among Ohio community pharmacists. *Pharmacy Practice (internet)*. 10 (3), 168–172.
- Rousseau, T., Anselem, O., Chantry, A.A., Lelong, N., Goffinet, F., 2021. Factors associated with inadequate folic acid supplementation for the prevention of neural tube defects in eight Parisian maternity units. *Gynecol. Obstet. Fert. Senol.* 49 (7–8), 573–579.
- Smith, A.D., Sobczyńska-Malefora, A., Green, R., Reynolds, E.H., Refsum, H., 2022. Mandatory food fortification with folic acid. *Lancet Global Health* 10 (10), e1389.
- Toivonen, K.I., Lacroix, E., Flynn, M., Ronksley, P.E., Oinonen, K.A., Metcalfe, A., et al., 2018. Folic acid supplementation during the preconception period: A systematic review and meta-analysis. *Preventive Med.* 114, 1–17.
- Tort, J., Lelong, N., Prunet, C., Khoshnood, B., Blondel, B., 2013. Maternal and health care determinants of preconceptional use of folic acid supplementation in France: results from the 2010 National Perinatal Survey. *BJOG: Int. J. Obstet. Gy.* 120 (13), 1661–1667.
- Viswanathan, M., Treiman, K.A., Kish-Doto, J., Middleton, J.C., Coker-Schwimmer, E.J. L., Nicholson, W.K., 2017. Folic acid supplementation for the prevention of neural tube defects: an updated evidence report and systematic review for the US preventive services task force. *JAMA*. 317 (2), 190–203.
- Wald, N.J., 2022. Folic acid and neural tube defects: Discovery, debate and the need for policy change. *J. Med. Screen.* 29 (3), 138–146.
- Wegner, C., Kancherla, V., Lux, A., Köhn, A., Bretschneider, D., Freese, K., et al., 2020. Periconceptional folic acid supplement use among women of reproductive age and its determinants in central rural Germany: Results from a cross sectional study. *Birth Defects Res.* 112 (14), 1057–1066.
- Williams, J., Mai, C.T., Mulinare, J., Isenburg, J., Flood, T.J., Ethen, M., et al., 2015. Updated estimates of neural tube defects prevented by mandatory folic Acid fortification - United States, 1995–2011. *MMWR Morb. Mortal Wkly. Rep.* 64 (1), 1–5.
- Yargawa, J., Leonardi-Bee, J., 2015. Male involvement and maternal health outcomes: systematic review and meta-analysis. *J. Epidemiol. Community Health.* 69 (6), 604–612.