European Journal of Clinical Nutrition
https://doi.org/10.1038/s41430-018-0255-2

BRIEF COMMUNICATION

Prevalence and determinants of folate deficiency among urban Indian women in the periconception period

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Received: 7 October 2017 / Revised: 6 June 2018 / Accepted: 8 June 2018

Abstract

Maternal folate insufficiency is of particular concern in developing countries due to its association with various adverse pregnancy outcomes. This study aimed to determine the prevalence of folate deficiency and its determinants among urban Indian women in the periconception period. Serum folate concentrations were measured in 584 women in early pregnancy (11 ± 3 weeks of gestation) using microbiological assay. Folate deficiency was detected in 24% women and possible deficiency was detected in 21% women. Multigravidity (aOR 1.84, 95% CI 1.16–2.92) and low education (aOR 1.67, 95% CI 1.06–2.62) emerged as determinants of folate deficiency while prenatal folic acid supplementation was favorable in decreasing the odds of folate deficiency (aOR 0.17, 95% CI 0.06–0.43). No association was observed between folate levels and adverse pregnancy outcomes including neural tube defects. The high prevalence of folate deficiency underlines the need for implementation of preconception folic acid supplementation as part of maternal health services in India.

Introduction

Folate deficiency is among the commonest micronutrient deficiencies worldwide and an issue of public health concern due to its crucial role in early development and growth of the fetus. However, the true magnitude of folate deficiency is unknown globally [1]. The main cause of folate deficiency is inadequate intake, an increased risk of which is especially high among pregnant women in resource poor settings [2]. Demographic and lifestyle factors including maternal age, body mass index (BMI), education level, socio-economic status, smoking, alcoholism and use of antifolate drugs have been associated with low folate concentrations [3].

In India, folic acid (FA), in the form of iron and FA supplementation is currently offered to pregnant women starting after the first trimester onwards as part of routine antenatal care services. There is, however no public health strategy for preconception FA supplementation. Data on the prevalence of folate deficiency in India is conflicting with reported prevalence rates ranging from 1.2% [4] to 26.3% [5]. There are limited Indian studies assessing folate deficiency during early pregnancy and no nationally representative data. In the current study, we report the prevalence of folate deficiency and selected characteristics that enhance the risk of folate deficiency among women recruited in the Pune Urban Birth Outcomes study (PUBOS). As reported earlier, the objective of PUBOS was to measure the birth prevalence of congenital anomalies [6].

Materials and methods

Blood samples were collected from 584 women at 11 ± 3 weeks of gestation presenting for antenatal care at government hospitals in Pune. There are currently no government guidelines on periconception folate supplementation. Data on the potential determinants of maternal folate status including maternal age, education, occupation, economic status, religion, gravidity, maternal BMI, anemia status, acute illness in the periconception period, underlying chronic illness, use of smokeless tobacco [7] was collected using a questionnaire. The methylenetetrahydrofolate reductase (MTHFR) 677C > T polymorphism [8] was

Electronic supplementary material The online version of this article (https://doi.org/10.1038/s41430-018-0255-2) contains supplementary material, which is available to authorized users.

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Published online: 19 July 2018

Table 1 Prenatal folic acid supplementation and folate deficiency

	Deficiency (<3 ng/ml) *N* (%)	Possible deficiency (3–5.9 ng/ml) *N* (%)	Normal (>5.9 ng/ml) *N* (%)
All ($n = 584$)	142 (24)	121 (21)	321 (55)
Reported use of prenatal FA supplements ($n = 83$)	10 (12.0)	9 (11)	64 (77)
Not taken any prenatal FA supplements ($n = 501$)	132 (26)	112 (22)	257 (51)

analyzed using standard methods. Data on adverse pregnancy outcomes were recorded as previously described [6]. Data on the use of any FA supplements in the periconception period, source of supplements, and compliance was recorded as reported by the women. The study was approved by the Ethics Committee of Savitribai Phule Pune University. Informed consent was obtained from the women at the time of recruitment in the study. All data collected were coded prior to use.

Measurement of serum folate concentrations

Two milliliters of blood was collected in serum separator tubes (Becton Dickinson, USA) for estimation of folate concentrations. Samples were anonymised and linked to the woman's coded socio-demographic and clinical data through a unique identifier. Serum was separated by centrifugation and stored at −80 °C protected from light till further analysis. For estimation of serum folate concentrations, samples were assayed using the ID-Vit® FA microbiological assay kit (Immundiagnostik AG, Germany) consisting of *Lactobacillus rhamnosus*-coated microtitre plates. Manufacturer's controls were used for assessing accuracy of the folate assay. Folate status was classified as: folate deficiency (<3 ng/ml), possible deficiency (3–5.9 ng/ml), and normal folate status (≥6 ng/ml) [9].

Statistical analysis

Determinants that showed significant association in univariate analysis were used in the multivariate analysis using a main-effects model to yield adjusted odds ratios. Significance was established at a two-sided p-value < 0.05. Statistical analyses were performed using Statistical Package for Social Sciences (SPSS) Version 17.0.

Results and discussion

Among 584 women, folate deficiency (serum folate concentration < 3 ng/ml) was present in 142 (24.3% (95% CI 21–27.9%) women and possible deficiency (3–5.9 ng/ml) was detected in 121 additional women (20.7%, 95% CI 17.6–24.2%) (Table 1). Among the 584 women, 501 women did not report taking any prenatal FA supplementation. Nearly half (244, 48.7%) of these women had some level of folate deficiency. Among 83 women who reported prenatal FA supplementation, 10 (12%) were folate deficient, 9 (11%) had possible folate deficiency, while 64 (77%) had normal folate concentrations. These women had been prescribed doses that ranged from 0.5 to 5 mg per day. Analysis of the data indicated that prenatal FA supplementation clearly decreased the odds of both folate deficiency (OR 0.17, 95% CI 0.07–0.39) and possible deficiency (OR 0.34, 95% CI 0.17–0.69) in the women.

Table 2 Determinants of folate status

Determinants	Deficiency (<3 ng/ml)		Possible deficiency (3–5.9 ng/ml)	
	aOR	**95% CI**	**aOR**	**95% CI**
Education				
>10 years	Ref		Ref	
≤10 years	1.67	1.06–2.62	1.60	1.02–2.50
Gravidity				
Primigravida	Ref			
Multigravida	1.84	1.16–2.92	–	–
Use of prenatal folic acid supplements				
No	Ref		Ref	
Yes	0.17	0.06–0.43	0.34	0.17–0.68

aOR adjusted odds ratio

The characteristics of 142 folate-deficient women and 121 women with possible folate deficiency were compared to those of 321 women with normal folate concentrations (Supplementary Table 1). Low education level, multigravidity, anemia, and prenatal FA supplementation emerged as significant determinants of folate deficiency in univariate analysis. After multivariate analysis, multigravidity (aOR 1.84, 95% CI 1.16–2.92) and low education (aOR 1.67, 95% CI 1.06–2.62) retained their significance and increased the odds of folate deficiency while prenatal FA supplementation decreased the odds of folate deficiency (aOR 0.17, 95% CI 0.06–0.43) (Table 2). In case of women with possible folate deficiency, low education increased the odds one and a half times (aOR 1.6, 95% CI 1.02–2.5) and

prenatal FA supplement use decreased the odds (aOR 0.34, 95% CI 0.17–0.68).

There was no significant association between folate concentrations and adverse pregnancy outcomes (Supplementary Table 2). Pregnancy outcome data was available for 530 (91%) women. Among these women, there were 496 (93.6%) live births, 15 (2.8%) stillbirths, and 17 (3.2%) miscarriages. In addition there were 8 (1.5%) pregnancies affected with a major congenital anomaly. The proportion of low birth weight and preterm births was 20% (95/474) and 12.7% (62/488), respectively. Compared to live births, women with folate deficiency were at an increased risk of having a stillbirth. Women with folate deficiency were also more likely to present with a congenital anomaly affected pregnancy. Unfortunately, due to the small sample, these associations were not statistically significant. Among the 83 women who had consumed prenatal FA supplements, pregnancy outcome data was available for 74 (89.2%) women. Of these, 72 (97.3%) women delivered live born babies and there was one stillbirth and termination of pregnancy each. Three (4.1%) women reported a congenital anomaly affected pregnancy.

The results of our study identify the high prevalence of folate deficiency among Indian women in the periconception period. Nearly a quarter of the women in this study had folate deficiency, and one-fifth had possible folate deficiency and were thus at an increased risk of becoming folate deficient in the near future. Another finding of this study was that multigravid women were at a higher risk of folate deficiency. The study offers two important findings for public health implementation. Firstly, the high prevalence of folate deficiency urges the need for incorporating preconception FA supplementation in the public health service for women in reproductive age in India. The other public health intervention is to reinforce the message of birth spacing, and the benefits of consuming a folate-rich diet in the intra-conception period. Unfortunately, periconception/intra-conception interventions are minimal in India, and other developing countries, as there are both logistic and financial challenges to implementing periconception interventions [10]. Data from this study, however, suggests that preconception and intra-conception interventions including advice on intake of preconception FA supplements needs to be seriously evaluated by the public health program providing maternal and child health services.

Acknowledgements The authors gratefully acknowledge Pune and Pimpri-Chinchwad municipal health authorities and the participating hospital staff for their support and help in conducting the study. The study was supported by the University Grant Commission-University with Potential for Excellence (UGC-UPE) Holistic area "Translation research in the health of women and children" Grant no. UGC-UPE 262 B(2) and the Departmental Research Development Program Fund of Savitribai Phule Pune University.

Funding The study was supported by the University Grants Commission-University with Potential for Excellence (UGC-UPE) Holistic area "Translation research in the health of women and children" Grant no. UGC-UPE 262 B(2) and the Departmental Research Development Program Fund of Savitribai Phule Pune University.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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