

BMJ Open Maternal adherence to micronutrient supplementation before and during pregnancy in Northwest China: a large-scale population-based cross-sectional survey

Danmeng Liu,¹ Yue Cheng,² Shaonong Dang,¹ Duolao Wang,³ Yaling Zhao,¹ Chao Li,¹ Shanshan Li,¹ Fangliang Lei,¹ Pengfei Qu,⁴ Baibing Mi,¹ Ruo Zhang,¹ Jiamei Li,⁵ Lingxia Zeng,¹ Hong Yan^{1,6,7}

To cite: Liu D, Cheng Y, Dang S, *et al.* Maternal adherence to micronutrient supplementation before and during pregnancy in Northwest China: a large-scale population-based cross-sectional survey. *BMJ Open* 2019;**9**:e028843. doi:10.1136/bmjopen-2018-028843

► Prepublication history for this paper is available online. To view these files please visit the journal online (<http://dx.doi.org/10.1136/bmjopen-2018-028843>).

LZ and HY contributed equally.

Received 27 December 2018

Revised 11 June 2019

Accepted 11 July 2019



© Author(s) (or their employer(s)) 2019. Re-use permitted under CC BY-NC. No commercial re-use. See rights and permissions. Published by BMJ.

For numbered affiliations see end of article.

Correspondence to

Professor Lingxia Zeng; tjlx@mail.xjtu.edu.cn

Professor Hong Yan; xjtu_yh.paper@aliyun.com

ABSTRACT

Objectives To report the situation of maternal micronutrient supplementation before and during pregnancy in Northwest China and to examine the rates of and factors related to the adherence to micronutrient supplementation among pregnant women in this region, where dietary micronutrient intake is commonly insufficient.

Design A large-scale population-based cross-sectional survey.

Setting Twenty counties and ten districts of Shaanxi Province.

Participants A sample of 30 027 women were selected using a stratified multistage random sampling method. A total of 28 678 women were chosen for the final analysis after excluding those who did not provide clear information about nutritional supplementation before and during pregnancy.

Main outcome measures Maternal adherence to micronutrient supplementation (high and low) were the outcomes. They were determined by the start time and duration of use according to Chinese guidelines (for folic acid (FA) supplements) and WHO recommendations (for iron, calcium and multiple-micronutrient (MMN) supplements).

Results In total, 83.9% of women took at least one kind of micronutrient supplement before or during pregnancy. FA (67.6%) and calcium (57.5%) were the primarily used micronutrient supplements; few participants used MMN (14.0%) or iron (5.4%). Adherence to supplementation of all micronutrients was low (7.4% for FA, 0.6% for iron, 11.7% for calcium and 2.7% for MMN). Higher educational levels, higher income levels, urban residence and better antenatal care (including pregnancy consultation and a higher frequency of antenatal visits) were associated with high adherence to micronutrient supplementation.

Conclusion Maternal micronutrient supplementation before and during pregnancy in Northwest China was way below standards recommended by the Chinese guidelines or WHO. Targeted health education and future nutritional guidelines are suggested to improve this situation,

Strengths and limitations of this study

- This is the first large-scale and representative study that vividly described maternal adherence to micronutrient supplementation before and during pregnancy in Northwest China.
- Sample representativeness in Shaanxi was guaranteed by a large sample of 28 678 women that were recruited using a stratified multistage random sampling method.
- The results could be generalised in Northwest China and may also reflect the universality of the problem in China and could serve as a basis for developing health education strategies in the future.
- Recall bias was ineluctable because the information was self-reported by retrospection.
- The study does not provide an insight into the dosage of specific micronutrient supplementation due to the uncertain specifications of some reported supplements.

especially in pregnant women with disadvantaged sociodemographic conditions.

INTRODUCTION

Pregnancy is a state in which macronutrient and micronutrient requirements increase due to maternal physiological changes and fetal growth.¹ During pregnancy, adequate micronutrient intake is difficult to achieve from daily diet,² and maternal micronutrient deficiencies could cause severe adverse outcomes, including stillbirth, low birth weight (LBW) and birth defects.³ Micronutrient supplementation is an alternative, in addition to the adjustment of diet pattern and quality, to fulfil the increased nutrition demands during pregnancy.⁴ In recent decades, maternal micronutrient

supplementation during pregnancy has attracted much attention, as growing evidence has shown that it has significant benefits in the improvement of maternal health status as well as birth outcomes.^{5–8} As a result, some micronutrients that greatly contribute to maternal and fetal health are highly recommended for routine use during pregnancy. Many countries have implemented periconceptional folic acid (FA) supplementation to protect against neural tube defects (NTDs).^{9–10} WHO has also provided several guidelines for micronutrient supplementation for pregnant women.¹¹ Daily use of FA (400 µg), starting from 2 months before the planned pregnancy to 12 weeks of pregnancy, is recommended for the prevention of NTDs;¹² daily oral FA combined with iron supplementation (400 µg FA and 30–60 mg iron) throughout pregnancy is recommended to reduce the risk of LBW, maternal anaemia and iron deficiency;¹³ daily oral calcium supplementation (1.5–2.0 g) in the second half of pregnancy is recommended for pregnant women in the area of low dietary calcium intake to reduce the risk of pre-eclampsia.¹⁴

China is the most populated developing country with a considerable incidence of adverse pregnancy outcomes, including maternal anaemia,¹⁵ LBW¹⁶ and small for gestational age (SGA).⁸ However, the implementation of FA supplementation project (take daily FA (400 µg), start from 3 months before pregnancy to the end of the first trimester) to prevent NTDs, especially in rural areas, is the only nutritional intervention promoted by the Chinese Health Ministry (now the Chinese National Health Commission) for pregnant women and women planning to be pregnant.^{17–18} Also, the only routine antenatal micronutrient supplementation recommended by the Chinese Nutrition Society (CNS) for women of childbearing age is the daily use of FA (400 µg), starting from 3 months before the planned pregnancy until the end of pregnancy.¹⁹ No more guidelines for routine supplementation of other micronutrients exist so that the use of micronutrient supplements during pregnancy varied in Chinese geographic areas and socioeconomic groups.^{4–20}

All health policies and recommendations of micronutrient supplementation for pregnant women emphasise the timing, dosage, sustainability of use as well as the target population. Evidence showed that low compliance was a major reason for the low effectiveness of micronutrient supplementation during pregnancy^{8–21} and thus the exploration of the determinants of the adherence is important for guiding the appropriate use to guarantee the efficacy. Many factors were reported in relation to maternal adherence to micronutrient supplementation before and during pregnancy, including maternal age, educational background, occupation and antenatal care. Previous studies have reported on the compliance of maternal micronutrient supplementation in Western countries like the USA and Norway^{22–23} as well as in Africa countries like Ethiopia and Kenya.^{24–25} Few of the studies focused on maternal adherence to micronutrient supplementation before and during pregnancy in China.

Shaanxi Province is a developing area in North-west China where most of the micronutrients derived from diet among pregnant women were lower than the Chinese recommended nutrient intake (RNI),^{26–27} especially the intake of folate and calcium.^{26–27} Although dietary iron intake was close to the RNI for the first and second trimester, most iron from diet were the non-heme iron, which is not efficiently absorbed and used by the human body.²⁸ Additionally, about 40% of women of childbearing age in the region suffered anaemia,²⁹ and the incidence of adverse birth outcomes, including LBW and preterm birth, was high in this region.³⁰ Therefore, maternal micronutrient supplementation seems to be a relatively inexpensive and low risk method for compensating for inadequate dietary intake during pregnancy and improving the health status of local mothers and fetus. However, a representative data from a large-scale study on the maternal micronutrient supplementation before and during pregnancy in this region are not available. Accordingly, this article aims to investigate the condition of maternal micronutrient supplementation before and during pregnancy in Shaanxi, focusing on analysing the rates and associated factors of maternal adherence to supplement consumptions according to existing recommendations and to provide evidence for future evaluation of health policy effectiveness and development of health education strategies.

METHODS

Data source and participants

The study used data from a large-scale population-based cross-sectional survey, which was conducted between August and November 2013 in the Shaanxi province with the purpose of investigating the prevalence and risk factors of birth defects among newborns, along with maternal dietary conditions and nutritional supplements use. The target population was women aged from 16 to 49 years, who were pregnant between 2010 and 2013 and had specific pregnancy outcomes before the survey. The sample was acquired from 20 counties and 10 districts of Shaanxi by applying a stratified multistage random sampling method.^{27–31} First, 20 counties and 10 districts were randomly selected from the 80 rural counties and 24 urban districts in Shaanxi Province according to the difference in size, distribution and fertility rates of population between rural and urban areas. Subsequently, in the rural area, 6 townships, 6 villages and 30 eligible women were randomly selected from each sampled county, selected township and selected village, respectively. In the urban areas, 3 streets, 6 communities and 60 eligible women were randomly selected from each sampled district, selected street and selected community, respectively. Data collection was completed with structured-questionnaires via in-person surveys by trained interviewers. Information gathered included maternal sociodemographic characteristics, lifestyle, health condition, healthcare utilisation and supplement consumption. A strict quality

control process was used to guarantee data integrity and accuracy.²⁷

A total of 30 027 women were enrolled in the survey after they signed the informed consent, and women with limited cognitive capacity had been excluded. In order to obtain more accurate analysis results, we further excluded 1349 women who did not provide clear information about maternal nutritional supplementation (among them, 761 women had no live birth babies in this pregnancy and refused to provide detailed information). In total, 28 678 women were chosen for the final analysis.

Maternal sociodemographic characteristics, parity and antenatal care information

Maternal age at delivery was divided into three categories (<25, 25–34 and ≥35 years), as well as educational level (Junior high school or below, Senior high school and College and beyond), geographical area (Southern Shaanxi, Central Shaanxi and Northern Shaanxi) and per capita annual household income (Low: <8800, Medium: 8800–15 200 and High: ≥15 200 Yuan, where 1 Yuan=\$0.149 on 17 March 2019). Residence (urban and rural) and parity (primiparous and multiparous) were classified into two categories each. We also investigated the antenatal care information, including the number of antenatal visits (<5 and ≥5), the type of hospitals for antenatal visit (hospitals below the county level and county level hospitals or above) and pregnancy consultation (yes and no, referred to the participation of health counselling that related to maternal healthcare and fetal development before or during pregnancy).

Micronutrient supplementation

Information about micronutrient supplements in tablet and capsule forms was mainly collected. We asked the participants to choose the supplements they used before or during pregnancy from a list of brands of supplements that were commonly provided in the local hospital or pharmacy and to further tell the brand and kind of supplement they consumed, if it was not shown in the list. We did not list iron-FA supplements in the questionnaire, since few supplements on the market were two-nutrient formulations of iron and FA. In the analysis, FA supplements referred to those that only contained FA; iron supplements referred to those that only contained iron; calcium supplements referred to those that contained calcium or calcium with another micronutrient (including calcium-vitamin D and calcium-zinc); multiple-micronutrient (MMN) supplements referred to those that contained FA, iron and other micronutrients. Women who consumed any micronutrient supplement before or during pregnancy were considered as micronutrient supplement users; otherwise, they were regarded as non-users.

We further obtained the time and duration of use of each supplement they reported. The participants were required to select the time of supplement use from the four pregnancy periods (3 months before the last menstrual period, the first trimester, the second trimester and the

third trimester) and report the duration of supplementation for each supplement they used. The 3 months before the last menstrual period was defined as the preconceptional period; the time from the 3 months before the last menstrual period to the end of first trimester was defined as the periconceptional period; the time of the second and third trimester was defined as the after-periconceptional period.

Adherence to micronutrient supplementation before and during pregnancy was determined by the start time and duration of use according to Chinese guidelines (for FA) and WHO recommendations (for iron, calcium and MMN). Although WHO did not universally recommend MMN supplementation (MMS) for pregnant women, due to its components of iron and FA, we still examined the compliance of MMS by referencing the WHO recommendation for iron and FA supplementation. We considered the duration of use instead of the total amounts, because most of the supplements of interest were taken as one tablet daily. In the present study, the thresholds used to define the adhered duration of use were 180 days for FA and 90 days for others. Therefore, high adherence to FA supplementation was defined as starting from the preconceptional period with ≥180 days of use; otherwise, it was regarded as low adherence. High adherence to iron supplementation was considered as starting from the first trimester with ≥90 days of use; otherwise, it was regarded as low adherence. For calcium supplementation, 20 weeks of gestation was the start time recommended by WHO. Since we did not collect the specific weeks of gestation of micronutrient supplementation, high adherence to calcium supplementation was considered as starting from the second trimester with ≥90 days of use; otherwise, it was regarded as low adherence. High adherence to MMS was defined as one starting from the first trimester with ≥90 days of use; otherwise, it was considered as low adherence.

Statistical analysis

Dataset was established using Epidata 3.1 (The Epidata Association, Odense, Denmark) with double entry. Multiple imputation was used to attribute values for the missing variables, including income level (n=5830), maternal age group (n=434) and the type of hospital for antenatal visits (n=327), taking education level, geographic area, residence, parity, the number of antenatal visits and pregnancy consultation as covariates with five imputed data sets.³² Numbers and percentages (n (%)) were estimated for reporting the rate of micronutrient supplementation in different groups and for presenting the adherence to micronutrient supplementation. Comparisons between groups were completed by either the χ^2 test or Fisher's exact test.

Because of the hierarchical structure of the data derived from the stratified multistage random sampling design, multivariable generalised estimating equation (GEE) models³³ with random effect at county level were applied to estimate adjusted OR and 95% CI for factors associated

with maternal adherence to micronutrient supplementation before and during pregnancy. Maternal characteristics including age, education, residence, income, parity, pregnancy consultation, number of antenatal visits and type of hospital for antenatal visits were the fixed effects in the GEE models. Binomial distribution, logit link function and an exchangeable covariance structure were used in the GEE analysis. Model 1 analysed the relationship between the adherence to micronutrient supplementation and the sociodemographic characteristics including age, education, residence and income. Model 2 analysed the relationship between the adherence to micronutrient supplementation and sociodemographic characteristics (all the variables in model 1), as well as parity and antenatal care characteristics. The criteria for statistical significance was $p < 0.05$. All analyses were performed using SAS V.9.4 (SAS Institute, Cary, North Carolina, USA).

RESULTS

Maternal characteristics according to micronutrient supplementation before and during pregnancy

Significant differences existed in aspects of maternal sociodemographic conditions, birth history and antenatal care characteristics between users and non-users of micronutrient supplements before and during pregnancy (table 1). Users of micronutrient supplements were more likely to be aged from 25 to 34 years, be better educated, have higher income level, live in central Shaanxi, be rural residents, be primiparous and have better antenatal care (including pregnancy consultations, higher-level hospital for antenatal visits and a higher frequency of antenatal visits).

Rates of and the adherence to micronutrient supplementation before and during pregnancy

In total, 83.9% of women took at least one kind of micronutrient supplement before or during their last pregnancy. The main supplements used by participants were FA (67.6%), calcium (57.5%), MMN (14.0%) and iron (5.4%) (table 2). Although FA had a relatively higher rate of use during the periconceptional period (64.5%), only 7.4% of women continued usage from the periconceptional period for longer than 180 days. Most of the users started taking calcium supplements during the second trimester (39%), but only 11.7% met the recommended standards after taking the duration of use into consideration. Comparing with the rates of those who began to use iron or MMN in the after-periconceptional period (3.7% for iron and 8.2% for MMN), smaller proportion of women started consumption from the first trimester (1.7% for iron and 5.8% for MMN) and few of them adhered to use of iron or MMN in more than 90 days (0.6% for iron and 2.7% for MMN) (table 3). We also found that very few women (0.2%) consumed FA and iron starting from the first trimester with more than 90 days of use (not shown in table). We further examined the adherence to supplementation of FA, iron and FA with iron by

taking the contribution of MMS into consideration. Still, the rates of compliant use were low (8.5% for FA, 3.2% for iron and 2.9% for FA with iron, not shown in table).

Factors associated with the adherence to micronutrient supplementation before and during pregnancy

Table 4 shows the results of multivariable GEE models. Higher educational levels (eg, FA: Senior high school vs Junior high school or below: OR 1.38, 95% CI 1.18 to 1.61; College and beyond vs Junior high school or below: OR 2.59, 95% CI 2.21 to 3.05), higher income levels (eg, FA: High vs Low: OR 1.27, 95% CI 1.11 to 1.45), urban residence (eg, FA: Urban vs Rural: OR 1.72, 95% CI 1.08 to 2.72) and better antenatal care (including pregnancy consultation (eg, FA: Yes vs No: OR 1.91, 95% CI 1.71 to 2.14) and a higher frequency of antenatal visits (eg, FA: ≥ 5 times vs < 5 times: OR 1.59, 95% CI 1.35 to 1.87)) were associated with high adherence to micronutrient supplementation before and during pregnancy. Compared with women below 25 years, women aged from 25 to 34 years were more likely to have high adherence to the supplementation of FA (OR 1.30, 95% CI 1.11 to 1.52), iron (OR 1.49, 95% CI 1.18 to 1.88) and MMN (OR 1.38, 95% CI 1.12 to 1.71). Women above 35 years were associated with a lower probability of high adherence to calcium supplementation (OR 0.71, 95% CI 0.62 to 0.81). Being multipara was less likely related to high adherence to FA supplementation (OR 0.70, 95% CI 0.58 to 0.84). The type of hospital for antenatal visits was not linked to the adherence to micronutrient supplementation.

DISCUSSION

In this large-scale cross-sectional study, we observed that micronutrient supplements were not used as commonly as expected before and during pregnancy, and maternal adherence to micronutrient supplementation among our population, particularly in women with sociodemographic-disadvantages, was low based on the CNS and WHO recommendations. Totally, the prevalence of maternal micronutrient supplementation before and during pregnancy in Shaanxi from 2010 to 2013 was 83.9%. Compared with other countries, our overall use rate was higher than that of USA from 1999 to 2006 (77.6%),² but lower than those of Sydney, Australia in 2014 (93.8%)³⁴ and Seoul, Korea in 2012 (88%).³⁵ Compared with the domestic data, it was similar to that of Sichuan Province (81.8%) in 2010⁴ and higher than the overall prevalence of eight Provinces of China in 2009 (66.4%).²⁰ FA, calcium, MMN and iron were the four supplements primarily used by participants.

Maternal FA supplementation is associated with the prevention of NTDs as well as the reduced risk of preterm delivery and SGA births.³⁶ Both WHO and CNS developed guidelines for promoting daily FA supplementation before and during pregnancy,^{13 19} and the Chinese government also implemented the periconceptional FA supplementation to prevent NTDs since 2009. In our

Table 1 Maternal characteristics according to micronutrient supplementation before and during pregnancy among Chinese women in Shaanxi, 2010–2013

Characteristics	Micronutrient supplementation				P value*
	Yes (n=24051)		No (n=4627)		
	n	%	n	%	
<i>Sociodemographic characteristics</i>					
Age (years)					<0.001
<25	7843	32.6	1615	34.9	
25–34	14299	59.5	2465	53.3	
≥35	1909	7.9	547	11.8	
Education					<0.001
Junior high school or below	14 113	58.7	3611	78.0	
Senior high school	5114	21.3	627	13.6	
College and beyond	4824	20.0	389	8.4	
Geographic area					<0.001
Southern Shaanxi	5099	21.2	776	16.8	
Central Shaanxi	13 731	57.1	1725	37.3	
Northern Shaanxi	5221	21.7	2126	45.9	
Residence					<0.001
Rural	15 846	65.9	3455	74.7	
Urban	8205	34.1	1172	25.3	
Per capita annual household income (RMB)					<0.001
Low	7990	33.2	1714	37.0	
Medium	7819	32.5	1604	34.7	
High	8242	34.3	1309	28.3	
<i>Birth history and antenatal care information</i>					
Parity					<0.001
Primiparous	14 651	60.9	2152	46.5	
Multiparous	9400	39.1	2475	53.5	
Pregnancy consultation†					<0.001
No	17 404	72.4	3981	86.0	
Yes	6647	27.6	646	14.0	
The number of antenatal visits					<0.001
<5	6310	26.2	2298	49.7	
≥5	17 741	73.8	2329	50.3	
Type of hospitals for antenatal visits					<0.001
Township hospitals	2783	11.6	622	13.4	
County hospitals or above	21 268	88.4	4005	86.6	

*P values for the differences among groups were derived from either the χ^2 tests or Fisher's exact test.

†Referred to the participation of health counselling that related to maternal healthcare and fetal development before or during pregnancy.

population, FA was the most popularly used supplement before and during pregnancy, but more than 30% of women still did not take it. Additionally, most of the users started to take FA supplements after they became pregnant and only few took FA supplements to prepare for pregnancy, which may indicate the high frequency of unplanned pregnancies or the lack of knowledge about

preconceptional FA supplementation. The more serious reality was that less than 10% of women adhered to FA supplementation preconceptionally in more than 180 days. Therefore, the use of FA supplements failed to reach the recommended standards among pregnant women in Northwest China, even when maternal routine FA supplementation was strongly promoted in China.

Table 2 Rates of maternal micronutrient supplementation before and during pregnancy among Chinese women in Shaanxi, 2010–2013

Micronutrient supplements	n	%
Folic acid	19352	67.6
Calcium	16414	57.5
Multiple micronutrient	4018	14.0
Iron	1547	5.4
Vitamin C	1147	4.0
B Vitamins	814	2.8
Vitamin E	173	0.6
Others*	1271	4.4

*Including vitamin A, vitamin D and fish oil.

China has a high prevalence of pregnancy anaemia, which is commonly caused by iron deficiency during pregnancy.^{15 37} Reviews stated that daily iron supplementation in pregnancy could be useful in improving iron status and birth outcomes.^{6 38} Only 5.4% of the participants consumed iron supplements during pregnancy, and the low rate of iron supplementation was possibly attributed to the lack of routine maternal iron supplementation guidelines in China and the popular use of antianaemic Chinese patent medicines among pregnant women in this region.³⁹ The proportion of women who had compliant iron supplementation was very low in our population (0.6% for iron and 3.2% for iron and iron-containing MMS), which is much lower than that of Western Amhara of Ethiopia (20.4% for FA-iron).²¹ On the basis of the WHO recommendation, maternal iron supplementation should be started as early as possible during pregnancy.¹³ Our participants usually began to use iron supplements after the periconceptional period rather than from the beginning of pregnancy. The reason may be that most women only took iron supplements under the direction of physicians after the occurrence of iron deficiency or iron deficiency anaemia during the second half of pregnancy, but prophylactic supplementation was very rare.

Maternal calcium supplementation has a clear beneficial effect on hypertension-related disorders during pregnancy and is possibly related to the reduction of preterm birth risk.⁴⁰ To prevent pre-eclampsia, WHO recommends daily calcium supplementation from 20 weeks of gestation for populations with low dietary calcium intake.¹⁴ From the background of the low dietary calcium intake among pregnant women (512 mg/d)²⁷ and the high prevalence of preterm birth,⁴¹ the WHO guideline may be suitable for widespread implementation in our population. A gap still exists between calcium supplementation among pregnant women in Northwest China and the WHO recommendation, according to the fact that more than 40% of women did not take calcium supplements during pregnancy and only 11.7% of the participants adhered to take

calcium right from the start of the second trimester for more than 90 days of use.

Evidence demonstrated that periconceptional MMS with iron and FA could promote maternal health status, reduce the risk of LBW, SGA and congenital abnormalities^{42 43} as well as improve the long-term intellectual development of offspring.⁴⁴ Developed countries like Australia had a high prevalence of periconceptional MMS (79.2%),³⁴ but the rate of MMS among our participants was 14.0%. WHO did not universally recommend MMS for pregnant women due to its potential neonatal mortality risks,¹¹ but the recent evidence showed no increased risk of neonatal mortality.^{43 45} Moreover, the 2016 WHO guidelines stated that 'policy-makers in populations with a high prevalence of nutritional deficiencies might consider the benefits of MMS on maternal health to outweigh the disadvantages and may choose to give MMS that include iron and folic acid'. Comprehensively taking the situations of Shaanxi (including high incidence of adverse birth outcomes, low intake of most micronutrients from daily diet as well as from supplements and disadvantaged sociodemographic conditions among many pregnant women) into consideration, to replace iron and FA with MMS for pregnant women in low-income areas might be a useful strategy to improve overall maternal micronutrient intake in this region.⁴³

When examining the factors associated with maternal adherence to micronutrient supplementation before and during pregnancy, we found that sociodemographic disadvantages and lower antenatal care level were associated with low adherence to micronutrient supplementation. Similar associations between educational level and prenatal health counselling with adherence to micronutrient supplementation were reported in literature.^{10 24 46} Our finding that higher age and primiparity were predictors of compliant use of FA was consistent with that of a previous study in Ireland.⁴⁷ We did not find any relationship between the type of hospital for antenatal visits and FA supplementation, which may reflect the balanced implementation of national health policy on maternal FA supplementation in the health system of the study region. In our population, higher frequency of antenatal visits was associated with higher adherence to micronutrient supplementation. Aside from routine obstetric examination, women accept the phased health education from the physicians during their antenatal care visits. In addition, women planning to be pregnant or are pregnant (before 12 weeks of gestation) can receive free FA provided by the Chinese government during antenatal care visits and learn to appropriately use them under professional guidance. Iron or calcium supplementation is usually recommended to pregnant women by physicians after the diagnosis of physical or pathological changes related to iron or calcium deficiency. For women with severe pregnancy reactions or MMN deficiency, the physician may recommend MMS. Thus, higher frequency of antenatal care visits provides more opportunities for women to learn and increases the possibilities for physicians to

Table 3 Maternal micronutrient supplementation recommendations from WHO and CNS; rates of main micronutrient supplementation by start time and duration of use and adherence to micronutrient supplementation before and during pregnancy among Chinese women in Shaanxi, 2010–2013

	FA (n=28 629)	Iron (n=28 644)	Calcium (n=28 548)	MMN (n=28 628)
<i>Recommendations</i>				
WHO recommendation	1.Purpose: NTDs prevention Settings: all Supplementation: daily use of FA (400 µg) Duration: start at 2 months before the planned pregnancy until 12 weeks of pregnancy 2.See recommendation for iron and FA supplementation in the right column	Purpose: pregnancy outcome improvement Settings: all Supplementation: daily use of iron (30–60 mg)-FA (400 µg) Duration: throughout pregnancy	Purpose: pre-eclampsia prevention Settings: areas with low calcium intake Supplementation: daily use of calcium (1.5–2.0 g) Duration: from 20 weeks' gestation until the end of pregnancy	N/A
CNS recommendation	Purpose: NTDs prevention and pregnancy outcome improvement Settings: all regions in China Supplementation: daily use of FA (400 µg) Duration: start at 3 months before the planned pregnancy until the end of pregnancy	No routine iron supplementation is recommended for pregnant women; Pregnant women with severe anaemia should appropriately take iron supplements under the guidance of physicians	N/A	N/A
<i>Micronutrient supplementation in our population (n (%))</i>				
Start at periconceptual period	18 469 (64.5)	499 (1.7)	5292 (18.5)	1665 (5.8)
Start at 3 month before pregnancy	4966 (17.4)	79 (0.3)	272 (1.0)	212 (0.8)
<90 days (180 days for FA)	3373 (11.8)	35 (0.1)	104 (0.4)	81 (0.3)
≥90 days (180 days for FA)	1593 (5.6)	44 (0.2)	168 (0.6)	131 (0.5)
Start at first trimester	13 503 (47.2)	420 (1.5)	5020 (17.6)	1453 (5.1)
<90 days (180 days for FA)	12 992 (45.4)	243 (0.9)	2291 (8.0)	683 (2.4)
≥90 days (180 days for FA)	511 (1.8)	177 (0.6)	2729 (9.6)	770 (2.7)
Start at after-periconceptual period	883 (3.1)	1048 (3.7)	11 122 (39.0)	2353 (8.2)
Start at second trimester	737 (2.6)	633 (2.2)	8947 (31.4)	1844 (6.4)
<90 days	524 (1.8)	454 (1.6)	5614 (19.7)	1238 (4.3)
≥90 days	213 (0.7)	179 (0.6)	3333 (11.7)	606 (2.1)
Start at third trimester	146 (0.5)	415 (1.5)	2175 (7.6)	508 (1.8)
<90 days	127 (0.4)	365 (1.3)	1810 (6.3)	435 (1.5)
≥90 days	19 (0.1)	50 (0.2)	365 (1.3)	73 (0.3)
<i>Adherence to micronutrient supplementation (n (%))*</i>				
Low adherence	26 525 (92.7)	28 467 (99.4)	25 215 (88.3)	27 858 (97.3)
High adherence	2104 (7.4)	177 (0.6)	3333 (11.7)	770 (2.7)

*High adherence to FA supplementation was defined as starting from the periconceptual period with ≥180 days of use; otherwise, it was regarded as low adherence. High adherence to iron supplementation was considered as starting from the first trimester with ≥90 days of use; otherwise, it was regarded as low adherence. High adherence to calcium supplementation was considered as starting from the second trimester with ≥90 days of use; otherwise, it was regarded as low adherence. High adherence to MMS was defined as starting from the first trimester with ≥90 days of use; otherwise, it was considered as low adherence. FA, folic acid; MMN, multiple-micronutrients; CNS, Chinese Nutrition Society.

know the pregnant women's health condition and to give recommendations in time, which finally promotes the adherence to micronutrient supplementation.

To the best of our knowledge, this is the first large-scale and representative study that investigated maternal micronutrient supplementation before and during pregnancy

Table 4 Rates of high adherence to micronutrient supplementation before and during pregnancy by maternal characteristics and adjusted OR (95% CI) for factors associated to the high adherence among Chinese women in Shaanxi, 2010–2013*

Characteristics	n	FA		Iron		Calcium		MMN	
		High adherence (%)†	Adjusted OR (95% CI)	High adherence (%)	Adjusted OR (95% CI)	High adherence (%)	Adjusted OR (95% CI)	High adherence (%)	Adjusted OR (95% CI)
Sociodemographic characteristics (Model 1)‡									
Age (years)									
<25	9458	5.3	Ref	0.4	Ref	11.2	Ref	1.7	Ref
25–34	16764	8.7	1.30 (1.11 to 1.52)§	0.7	1.49 (1.18 to 1.88)§	12.4	1.03 (0.94 to 1.12)	3.3	1.38 (1.12 to 1.71)§
≥35	2456	6.3	1.22 (0.98 to 1.51)	0.6	1.54 (0.80 to 2.99)	8.6	0.71 (0.62 to 0.81)§	2.3	1.24 (0.84 to 1.84)
Education									
Junior high school or below	17724	4.9	Ref	0.4	Ref	9.9	Ref	1.6	Ref
Senior high school	5741	7.3	1.38 (1.18 to 1.61)§	0.9	2.00 (1.36 to 2.96)§	13.8	1.32 (1.22 to 1.42)§	2.8	1.51 (1.21 to 1.88)§
College and beyond	5213	15.9	2.59 (2.21 to 3.05)§	1.2	1.69 (1.12 to 2.54)§	15.5	1.45 (1.31 to 1.60)§	6.2	2.65 (2.14 to 3.28)§
Residence									
Rural	19301	5.9	Ref	0.4	Ref	10.6	Ref	2.1	Ref
Urban	9377	10.4	1.72 (1.08 to 2.72)§	1.1	1.88 (1.17 to 3.01)§	14.0	1.21 (0.90 to 1.62)	3.9	1.30 (0.82 to 2.06)
Per capita annual household income (RMB)									
Low	9689	5.0	Ref	0.4	Ref	10.6	Ref	1.8	Ref
Medium	9402	6.4	1.07 (0.94 to 1.23)	0.5	1.06 (0.74 to 1.54)	11.7	1.08 (0.99 to 1.19)	2.2	1.18 (0.96 to 1.45)
High	9538	10.7	1.27 (1.11 to 1.45)§	1.0	1.56 (1.05 to 2.32)§	12.8	1.09 (0.96 to 1.24)	4.0	1.39 (1.11 to 1.76)§
Birth history and antenatal care information (Model 2)¶									
Parity									
Primiparous	16803	9.2	Ref	0.7	Ref	12.8	Ref	3.2	Ref
Multiparous	11875	4.8	0.70 (0.58 to 0.84)§	0.5	0.90 (0.61 to 1.34)	10.1	1.02 (0.94 to 1.11)	1.9	0.88 (0.72 to 1.07)
pregnancy consultation									
No	21385	5.6	Ref	0.5	Ref	10.7	Ref	2.3	Ref
Yes	7293	12.6	1.91 (1.71 to 2.14)§	1.0	1.40 (1.21 to 1.96)§	14.7	1.22 (1.10 to 1.34)§	3.8	1.40 (1.17 to 1.67)§
The number of antenatal visits									
<5	8608	3.8	Ref	0.3	Ref	7.6	Ref	15.4	Ref
≥5	20070	8.9	1.59 (1.35 to 1.87)§	0.8	1.66 (1.18 to 2.34)§	13.4	1.41 (1.25 to 1.60)§	26.4	1.33 (1.09 to 1.62)§
Type of hospitals for antenatal visits									
Township hospitals	3405	5.9	Ref	0.5	Ref	9.6	Ref	1.7	Ref
County hospitals or above	25273	7.6	1.14 (0.94 to 1.37)	0.6	1.26 (0.79 to 2.01)	12.0	1.10 (0.94 to 1.29)	2.8	1.14 (0.90 to 1.46)

Continued

Table 4 Continued

Characteristics	n	FA		Iron		Calcium		MMN	
		High adherence (%)†	Adjusted OR (95% CI)	High adherence (%)	Adjusted OR (95% CI)	High adherence (%)	Adjusted OR (95% CI)	High adherence (%)	Adjusted OR (95% CI)

*N=28678. The number of missing values for supplementation of FA, iron, calcium and MMN were 49, 34, 130 and 50. Adjusted OR and 95% CI were derived from multivariable GEE models with random effects at county level.

†High adherence to FA supplementation was defined as starting from the periconceptional period with ≥180 days of use; high adherence to iron supplementation was considered as starting from the first trimester with ≥90 days of use; high adherence to calcium supplementation was considered as starting from the second trimester with ≥90 days of use; high adherence to MMS was defined as starting from the first trimester with ≥90 days of use.

‡Model 1 adjusted for the sociodemographic characteristics including maternal age, education, residence and income and the OR and 95% CI of these characteristics was derived from model 1.

§Model 2 adjusted for all variables in model 1 plus parity and antenatal care characteristics, and the OR and 95% CI of parity and antenatal care characteristics were derived from model 2.

¶Refers to p<0.05.

FA, folic acid; GEE, generalised estimating equation; MMN, multiple-micronutrients.

in Northwest China. To guarantee the representativeness, a large sample was recruited from Shaanxi Province of Northwest China using a stratified multistage random sampling method according to the proportion of rural to urban residents, population size and fertility rate in the region. The results could be generalised to other regions in Northwest China according to the similarities in terms of economy, culture, lifestyle and diet habits existing in these regions and may also reflect the universality of the low adherence to micronutrient supplementation before and during pregnancy in China. Therefore, it could serve as a basis for developing health education strategies in the future. Nonetheless, several limitations of the present study should be stated. First, this study was retrospective and all the information of micronutrient supplementation was self-reported from participants and therefore recall bias was ineluctable. Second, we did not provide an insight into the dosage of use. Although we listed the possible brands of supplements that women might consume, many women could only recall the micronutrient they used without clear commodity information. Except for FA supplements, which usually have specified dosage of 400 µg per pill, the specifications of other supplements vary from each other and thus it is difficult to calculate the accurate dosage used by our participants. However, what is certain is that some supplements women consumed were not specialised for pregnant women and thus the content of elemental iron or calcium in one tablet of the supplement is lower than the WHO recommended dosage, which may indicate the more severe situation of low adherence of micronutrient supplementation in our population. Third, the sources of recommendation regarding the use of supplements, as well as the access that women procured the supplements, were not recorded. Hence, the approach for more appropriate future interventions could not be known. More large-scale, in-depth and well-designed studies are recommended to explore the effectiveness of supplementation of iron, calcium and MMN on pregnancy outcomes according to the adherence of use and further promote the establishment of new nutritional recommendations for pregnancy in China.

CONCLUSION

In conclusion, maternal micronutrient supplementation before and during pregnancy in Shaanxi failed to meet the Chinese guidelines and WHO recommendation, with respect to start time and duration of use. Improving the adherence to micronutrient supplementation before or during pregnancy is still a dire issue for maternal and child health in Northwest China. Targeted health education and future guidelines of micronutrient supplementation for pregnant women should be implemented, especially for those with disadvantaged sociodemographic conditions.

Author affiliations

¹Department of Epidemiology and Health Statistics, Xi'an Jiaotong University Health Science Center, Xi'an, China

²Department of Nutrition, Xi'an Jiaotong University Health Science Center, Xi'an, China

³Liverpool School of Tropical Medicine, Liverpool University, Pembroke Place, UK

⁴Translational Medicine Center, Northwest Women's and Children's Hospital, Xi'an, China

⁵Department of Emergency Medicine, the Second Affiliated Hospital of Xi'an Jiaotong University, Xi'an, China

⁶Nutrition and Food Safety Engineering Research Center of Shaanxi Province, Xi'an, China

⁷Key Laboratory of Environment and Genes Related to Diseases, Xi'an Jiaotong University, Ministry of Education, Xi'an, China

Acknowledgements The authors are grateful to all women who took part in this research, all health staff who coordinated fieldwork and all investigators who contributed to data collection.

Contributors DL, YC, LZ and HY conceived and designed the study. DL, SL, FL, BM, RZ and JL collected and cleared the data. DL, DW, YZ, CL, SL, FL and PQ analysed and interpreted the data. DL, YC, SD and LZ drafted and revised the manuscript. All authors read and approved the final version of the manuscript.

Funding This work was supported by the National Natural Science Foundation of China (grant number 81230016 and 81202218) and Shaanxi Health and Family Planning Commission (grant number Sxwsjzswzfcg2016-013).

Competing interests None declared.

Patient and public involvement statement No patients were involved in developing the research question, outcome measure and design of the study. We were unable to disseminate the results of the research directly to study participants, and we informed the results to the local health authorities.

Patient consent for publication Not required.

Ethics approval This study was approved by the Ethic Review Committee and Academic Committee of Xi'an Jiaotong University Health Science Center (Approval No. 2012008). Written informed consent was obtained from all participants.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement No additional data are available.

Open access This is an open access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited, appropriate credit is given, any changes made indicated, and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>.

REFERENCES

1. Imdad A, Yakoob MY, Bhutta ZA. The effect of folic acid, protein energy and multiple micronutrient supplements in pregnancy on stillbirths. *BMC Public Health* 2011;11(Suppl 3):S4.
2. Branum AM, Bailey R, Singer BJ. Dietary supplement use and folate status during pregnancy in the United States. *J Nutr* 2013;143:486–92.
3. Gernand AD, Schulze KJ, Stewart CP, et al. Micronutrient deficiencies in pregnancy worldwide: health effects and prevention. *Nat Rev Endocrinol* 2016;12:274–89.
4. Tang L, Lee AH, Yau KKW, et al. Consumption of dietary supplements by Chinese women during pregnancy and postpartum: a prospective cohort study. *Matern Child Nutr* 2017;13. 10.1111/mcn.12435
5. Hofmeyr GJ, Lawrie TA, Atallah Álvaro N, et al. Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. *Cochrane Database Syst Rev* 2014;3 Suppl 1.
6. Peña-Rosas JP, De-Regil LM, Garcia-Casal MN, et al. Daily oral iron supplementation during pregnancy. *Cochrane Database Syst Rev* 2015;170.
7. De-Regil LM, Peña-Rosas JP, Fernández-Gaxiola AC, et al. Effects and safety of periconceptional oral folate supplementation for preventing birth defects. *Cochrane Database Syst Rev* 2015;(12):Cd007950.
8. Li N, Li Z, Ye R, et al. Impact of periconceptional folic acid supplementation on low birth weight and small-for-gestational-age infants in China: a large prospective cohort study. *J Pediatr* 2017;187:105–10.
9. Bibbins-Domingo K, Grossman DC, Curry SJ, et al. Folic acid supplementation for the prevention of neural tube defects: US preventive services Task force recommendation statement. *JAMA* 2017;317:183–9.
10. Teixeira JA, Castro TG, Wall CR, et al. Determinants of folic acid supplement use outside national recommendations for pregnant women: results from the growing up in New Zealand cohort study. *Public Health Nutr* 2018;21:2183–92.
11. WHO. *WHO Recommendations on Antenatal Care for a Positive Pregnancy Experience*. Geneva, Switzerland: World Health Organization, 2016.
12. WHO. Prevention of neural tube defects standards for maternal and neonatal care, 2007. Available: https://www.who.int/reproductivehealth/publications/maternal_perinatal_health/a91272/en/
13. WHO. *Guideline: daily iron and folic acid supplementation in pregnant women*. Geneva: World Health Organization, 2012.
14. WHO. *Guideline: calcium supplementation in pregnant women*. Geneva: World Health Organization, 2013.
15. WHO. *Worldwide prevalence of anaemia 1993–2005: who global database on anaemia*, 2008: 1–51.
16. Zeng L, Dibley MJ, Cheng Y, et al. Impact of micronutrient supplementation during pregnancy on birth weight, duration of gestation, and perinatal mortality in rural Western China: double blind cluster randomised controlled trial. *BMJ* 2008;337.
17. Berry RJ, Li Z, Erickson JD, et al. Prevention of neural-tube defects with folic acid in China. China-U.S. Collaborative project for neural tube defect prevention. *N Engl J Med* 1999;341:1485–90.
18. NHC of the People's Republic of China. Notifications on the issuance of "program of folic acid supplementation for the prevention of neural tube defects", 2009. Available: <http://www.nhfpc.gov.cn/tigs/s9660/200906/fac102b5c5a471788f8b8a8eed09a31.shtml>
19. Chinese Nutrition Society. *Chinese dietary guidelines*. Tibet people's Press, 2013: 116–31.
20. Wang J, Zhao L, Piao J, et al. [Nutrition and health status of pregnant women in 8 provinces in China]. *Wei Sheng Yan Jiu* 2011;40:201–3.
21. Taye B, Abeje G, Mekonen A. Factors associated with compliance of prenatal iron folate supplementation among women in Mecha district, Western Amhara: a cross-sectional study. *Pan Afr Med J* 2015;20.
22. Jasti S, Siega-Riz AM, Cogswell ME, et al. Pill count adherence to prenatal multivitamin/mineral supplement use among low-income women. *J Nutr* 2005;135:1093–101.
23. Nordeng H, Eskild A, Nesheim B-I, et al. Guidelines for iron supplementation in pregnancy: compliance among 431 parous Scandinavian women. *Eur J Clin Pharmacol* 2003;59:163–8.
24. Gebreamlak B, Dadi AF, Atnafu A. High adherence to Iron/Folic acid supplementation during pregnancy time among antenatal and postnatal care attendant mothers in governmental health centers in Akaki Kality sub City, Addis Ababa, Ethiopia: hierarchical negative binomial poisson regression. *PLoS One* 2017;12:e0169415.
25. Kamau MW, Mirie W, Kimani S. Compliance with iron and folic acid supplementation (IFAS) and associated factors among pregnant women: results from a cross-sectional study in Kiambu County, Kenya. *BMC Public Health* 2018;18:580.
26. Cheng Y, Dibley MJ, Zhang X, et al. Assessment of dietary intake among pregnant women in a rural area of Western China. *BMC Public Health* 2009;9:222.
27. Yang J, Dang S, Cheng Y, et al. Dietary intakes and dietary patterns among pregnant women in northwest China. *Public Health Nutr* 2017;20:282–93.
28. Yang J, Cheng Y, Pei L, et al. Maternal iron intake during pregnancy and birth outcomes: a cross-sectional study in northwest China. *Br J Nutr* 2017;117:862–71.
29. Dang SN, Yan H, Xing Y. [Study on the level of hemoglobin and folate and anemia among women of childbearing age in Shaanxi, China]. *Zhonghua Liu Xing Bing Xue Za Zhi* 2008;29:515–6.
30. Wang LL, Bai RH, Liu Q, et al. [Epidemiological study on adverse pregnancy outcomes in Shaanxi province]. *Zhonghua Liu Xing Bing Xue Za Zhi* 2016;37:1379–82.
31. Pei L, Kang Y, Cheng Y, et al. The association of maternal lifestyle with birth defects in Shaanxi Province, northwest China. *PLoS One* 2015;10:e0139452.
32. Sterne JAC, White IR, Carlin JB, et al. Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. *BMJ* 2009;338:b2393.
33. Hubbard AE, Ahern J, Fleischer NL, et al. To Gee or not to Gee: comparing population average and mixed models for estimating the associations between neighborhood risk factors and health. *Epidemiology* 2010;21:467–74.
34. Shand AW, Walls M, Chatterjee R, et al. Dietary vitamin, mineral and herbal supplement use: a cross-sectional survey of before and during

- pregnancy use in Sydney, Australia. *Aust N Z J Obstet Gynaecol* 2016;56:154–61.
35. Kim H, Jang W, Kim K-N, *et al.* Comparison of dietary food and nutrient intakes by supplement use in pregnant and lactating women in Seoul. *Nutr Res Pract* 2013;7:199–206.
 36. Zhang Q, Wang Y, Xin X, *et al.* Effect of folic acid supplementation on preterm delivery and small for gestational age births: a systematic review and meta-analysis. *Reproductive Toxicology* 2017;67:35–41.
 37. McLean E, Cogswell M, Egli I, *et al.* Worldwide prevalence of anaemia, who vitamin and mineral nutrition information system, 1993–2005. *Public Health Nutr* 2009;12:444–54.
 38. Haider BA, Olofin I, Wang M, *et al.* Anaemia, prenatal iron use, and risk of adverse pregnancy outcomes: systematic review and meta-analysis. *BMJ* 2013;346:f3443.
 39. Liu DM, JM L, PF Q, *et al.* Prenatal supplementations of iron, iron-containing multimicronutrients and antianemic Chinese patent medicines in women in Shaanxi province, 2010–2013]. *Zhonghua Liu Xing Bing Xue Za Zhi* 2017;38:1466–70.
 40. Hofmeyr GJ, Lawrie TA, Atallah AN, *et al.* Calcium supplementation during pregnancy for preventing hypertensive disorders and related problems. *Cochrane Database Syst Rev* 2018;10.
 41. Zou L, Wang X, Ruan Y, *et al.* Preterm birth and neonatal mortality in China in 2011. *Int J Gynaecol Obstet* 2014;127:243–7.
 42. Czeizel AE. Periconceptional folic acid and multivitamin supplementation for the prevention of neural tube defects and other congenital abnormalities. *Birth Defect Res A* 2009;85:260–8.
 43. Haider BA, Bhutta ZA, Cochrane Pregnancy and Childbirth Group. Multiple-micronutrient supplementation for women during pregnancy. *Cochrane Database Syst Rev* 2017;30.
 44. Zhu Z, Cheng Y, Zeng L, *et al.* Association of antenatal micronutrient supplementation with adolescent intellectual development in rural Western China: 14-year follow-up from a randomized clinical trial. *JAMA Pediatr* 2018;172:832–41.
 45. Sudfeld CR, Smith ER. New evidence should inform who guidelines on multiple micronutrient supplementation in pregnancy. *J Nutr* 2019;149:359–61.
 46. Bixenstine PJ, Cheng TL, Cheng D, *et al.* Association between preconception counseling and folic acid supplementation before pregnancy and reasons for non-use. *Matern Child Health J* 2015;19:1974–84.
 47. Cawley S, Mullaney L, McKeating A, *et al.* An analysis of folic acid supplementation in women presenting for antenatal care. *J Public Health* 2016;38:122–9.