Original Article

The different effects of prenatal nutrient supplementation on neonatal birth weights between urban and rural areas of northwest China: a cross-sectional study

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Background and Objectives: The results of prenatal nutrient supplementation on birth weight are inconsistent in different areas. This study aimed to investigate whether the effects of prenatal iron plus folic acid and folic acid supplementation on neonatal birth weights differed between urban and rural areas of Northwest China. **Methods and Study Design:** A stratified multistage random sampling method was used to recruit women between the ages of 15 and 49 and their offspring born between 2010 and 2013 from 10 urban areas and 20 rural areas of the Shaanxi Province of Northwest China. Information regarding socio-demographics and prenatal nutrient supplementation status was collected using a standardized questionnaire, and the neonatal birth weights were obtained from the birth certificates. Multilevel models were established separately for the urban and rural areas to assess the effects of prenatal nutrient supplementation on neonatal birth weights. **Results:** The association between prenatal nutrient supplementation and neonatal birth weight was not statistically significant in urban areas. However, in rural areas, prenatal iron plus folic acid and folic acid supplementation increased the mean birth weights by 45.3 g (9.4 to 81.1 g, p=0.014) and 30.9 g (15.6 to 46.1 g, p<0.001), respectively. **Conclusions:** The effects of prenatal nutrient supplementation on neonatal birth weights differ between urban and rural areas of Northwest China. The different effects may be due to the different nutritional status of the urban and rural pregnant women. Prenatal nutrient supplementation may be a helpful way for improving neonatal birth weight in rural areas.

Key Words: prenatal nutrient supplementation, neonatal birth weight, different effects, northwest China, cross-sectional study

INTRODUCTION

Birth weight as an indicator of foetal growth is closely related to neonatal survival and health.[1,2] In the long run, birth weight may also be associated with health, educational attainment and income later in life.[3] To ensure a healthy baby, prenatal nutrient supplementation is often prescribed.[4] However, the effects of prenatal iron plus folic acid (IFA) and folic acid (FA) supplementation on neonatal birth weights are inconsistent in different areas.[5-8]

A national population-based survey undertaken in Zimbabwe showed that prenatal IFA supplementation significantly increased neonatal birth weights.[5] However, another nationally representative, cross-sectional survey in India showed that, compared with non-users, IFA supplementation was not associated with birth weight after adjustment for antenatal care (ANC) visits.[6] Some studies have reported positive effects of prenatal FA supplementation on birth weights.[7] However, a prospective cohort study in the USA showed no significant association between prenatal FA supplementation and low birth weights.[8]

According to previous studies in China, there are huge differences in socio-demographics and other characteristics between urban and rural areas.[9-13] In this study, we investigated whether the effects of prenatal IFA and FA supplementation on neonatal birth weights differed between urban and rural areas of Northwest China.

METHODS

Study design and participants

This cross-sectional study was conducted from August to

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November of 2013. According to the proportion of urban to rural residents, fertility rate and population size in Shaanxi Province of Northwest China, women between the ages of 15 and 49 and their offspring born between 2010 and 2013 from 10 urban areas and 20 rural areas were recruited by using a stratified multistage and random sampling method. The details have been described elsewhere.[14] This study was supported by the Ministry of Health of the Shaanxi Province, the local maternal and child health hospitals, the local village clinics and the community health service centres.

A questionnaire designed by the Xi'an Jiaotong University Health Science Center was utilized. Trained, skilled interviewers from the Faculty of Public Health of Xi'an Jiaotong University collected information regarding the neonates and the women's socio-demographic characteristics, lifestyle, health condition, healthcare utilization and nutrient supplementation during pregnancy. Cases involving multiple births, stillbirth, abortion, odinopoeia or new-borns without recorded birth weights were excluded.

Main outcome

The main outcome of this study was neonatal birth weight, which was obtained from the birth certificates and operationalized as a continuous variable.

Prenatal nutrient supplement assessment

From 3 months before conception up to and including all months of pregnancy, women who used iron plus folic acid were included in the IFA group, and women who used any supplements containing folic acid alone were included in the FA group. Those who used neither iron nor folic acid were defined as non-users.

Socio-demographic characteristics

The urban and rural classification in this study was defined according to China's household registration system. Information regarding demographics (neonatal sex, gestational age, maternal childbearing age, marital status, education, and so on), healthcare utilization (time of the first ANC visit and number of ANC visits), lifestyle (second-hand smoke exposure), and health conditions (gestational hypertension and anaemia) during pregnancy were collected using a standardized interview questionnaire. Gestational age was divided into two categories (<37 weeks and ≥37 weeks), maternal childbearing age was divided into three categories (<20 years, 20-34 years and ≥35 years), marital status was divided into two categories (married and other), maternal education was divided into three levels (primary school or lower, secondary school and senior school or higher), and maternal employment status was divided into two categories (employed and unemployed). The participants' economic level was categorized into three groups according to the tertiles of per capita annual household income (<8,000 Yuan, 8,000-15,999 Yuan and ≥16,000 Yuan, where 1 Yuan = $US 0.15 on 11 February 2017). Parity was divided into two categories (1 and ≥2), and the time of the first ANC visit was divided into two categories (≤12 weeks and >12 weeks). The number of ANC visits as a reflection of maternal access to healthcare was divided into two categories (<5 visit and ≥5 visit). Second-hand smoke exposure was defined as inhaling another person's tobacco smoke for more than 15 minutes per day.[15] Gestational hypertension and anaemia were assessed based on whether the participants had been diagnosed by doctors during pregnancy.

Statistical analysis

All data were double entered using Epidata version 3.1 (The Epidata Association, Odense, Denmark). Categorical variables were described using n (%) and compared by chi-square tests. Continuous variables were described using mean (SD) and compared by t test for two groups.

Since we used the stratified multi-stage random sampling method, the multilevel model approach was a good method for analysing the data with a hierarchical structure. After running the empty models, the intra-class correlation (ICC) was 0.01 (p<0.001) for urban areas and 0.01 (p<0.001) for rural areas. This indicated that there was homogeneity in the neonatal birth weights both in urban and rural areas.

Therefore, instead of Ordinary Least Square (OLS) regression, the relationships among prenatal nutrient supplementation, other covariates, and neonatal birth weight were examined using the multilevel model. With areas set to level 2 and individuals set to level 1, we established the 2-level models for the urban and rural areas separately. In each 2-level model, the non-users were set as the reference, and the estimated difference (Diff) and 95% confidence interval (CI) of birth weight were calculated for the IFA and FA groups. Five models were established to control for covariates step by step. Model 1 was not adjusted for any variable. Model 2 was adjusted for socio-demographic characteristics including neonatal sex, gestational age, maternal childbearing age, marital status, education, employment, per capita annual household income and parity. Model 3 was adjusted for all of the variables in Model 2, as well as health care utilization, including time of the first ANC visit and number of ANC visits. Model 4 was adjusted for all of the variables in Model 3, as well as prenatal lifestyle, including second-hand smoke exposure. Model 5 was adjusted for all of the variables in Model 4, as well as health conditions during pregnancy, including gestational hypertension and anaemia during pregnancy.

All of the statistical analyses were performed using the Statistical Analysis Systems statistical software package, version 9.3 (SAS Institute, Cary, NC, USA). A two-tailed p<0.05 was considered statistically significant.

Ethics statement

This study complied with the Declaration of Helsinki and was approved by the Ethics Committee of Xi'an Jiaotong University Health Science Center (No. 20120008). Written informed consent with the purpose, process and confidentiality of the study were obtained from all the participants.

RESULTS

Characteristics of the participants

In total, 5,742 women in urban areas and their single live births, as well as 21,847 women in rural areas and their single live births, were enrolled in this study after the exclusion of those who refused to participate (n=2,374), those with multiple births (n=349), those who experienced miscarriages or stillbirths (n=756), those with missing neonatal birth weights (n=199), and those with missing information regarding prenatal nutrient supplementation (n=1,133). The socio-demographic characteristics, reproductive history, healthcare utilization, lifestyles, health conditions during pregnancy and nutrient supplementation were significantly different between the two areas (Table 1). Compared with the women in rural areas, a higher proportion of the women in urban areas were of childbearing age (between 20-34 years) (90.4% vs 88.0%), and a lower proportion was unmarried (1.4% vs 2.3%).

Table 1. Characteristics of the study participants by area†

Characteristics	Urban (n=5,742)	Rural (n=21,847)	*p*-value‡
Neonatal characteristics			
Neonatal sex, n (%)			0.003
male	3,023 (52.7)	11,977 (54.8)	
female	2,719 (47.3)	9,870 (45.2)	
Gestational age, n (%)			0.243
<37 weeks	173 (3.0)	596 (2.7)	
≥37 weeks	5,569 (97.0)	21,251 (97.3)	
Socio-demographic characteristics			
Childbearing age, n (%)§			<0.001
<20 years old	55 (1.0)	637 (2.9)	
20-34 years old	5,191 (90.4)	19,225 (88.0)	
≥35 years old	369 (6.4)	1,689 (7.7)	
Marital status, n (%)§			<0.001
Married	5,656 (98.5)	21,309 (97.5)	
Other	82 (1.4)	504 (2.3)	
Maternal education, n (%)§			<0.001
Primary school or lower	181 (3.2)	3,098 (14.2)	
Secondary school	1,059 (18.4)	12,600 (57.7)	
Senior school or higher	4,497 (78.3)	6,105 (27.9)	
Maternal employment status, n (%)§			<0.001
Employed	3,822 (66.6)	5,582 (25.6)	
Unemployed	1,885 (32.8)	16,135 (73.9)	
Per capita annual household income, n (%)§			<0.001
<8,000 yuan	332 (5.8)	6,866 (31.4)	
8,000-15,999 yuan	1,350 (23.5)	6,801 (31.1)	
≥16,000 yuan	3,402 (59.3)	4,349 (19.9)	
Reproductive History			
Parity, n (%)			<0.001
1	4,549 (79.2)	11,610 (53.1)	
≥2	1,193 (20.8)	10,237 (46.9)	
Healthcare utilization			
Time of the first ANC visit, n (%)§			<0.001
≤12 weeks	5,020 (87.4)	18,232 (83.5)	
>12 weeks	634 (11.0)	3,129 (14.3)	
Number of ANC visits, n (%)§			<0.001
<5	1,136 (19.8)	7,276 (33.3)	
≥5	4,494 (78.3)	14,252 (65.2)	
Lifestyles			
Second-hand smoke exposure, n (%)§			<0.001
Yes	981 (17.1)	5,297 (24.3)	
No	4,699 (81.8)	16,027 (73.4)	
Health conditions			
Gestational hypertension, n (%)§			0.076
Yes	105 (1.8)	328 (1.5)	
No	5,630 (98.1)	21,488 (98.4)	
Anaemia, n (%)§			<0.001
Yes	661 (11.5)	3,398 (15.6)	
No	5,066 (88.2)	18,394 (84.2)	
Nutrient supplementation, n (%)			<0.001
IFA	550 (9.6)	902 (4.1)	
FA	3,981 (69.3)	13,711 (62.8)	
Non-users	1,211 (21.1)	7,234 (33.1)	

ANC: antenatal care; FA: folic acid; IFA: iron plus folic acid.

†Values are presented as n (%) for these categorical variables.

‡*p* values for differences between groups were derived from the chi-square test for categorical variables.

§The number of missing values for childbearing age, marital status, maternal education, maternal employment status, per capita annual household income, time of the first ANC visit, number of ANC visit, exposed to second-hand smoke, gestational hypertension and anemia was 423, 38, 49, 165, 4 489, 431, 574, 585, 38 and 70, respectively.

They were well educated (senior school or higher: 78.3% vs 27.9%) and more likely to be employed (66.6% vs 25.6%). They were also richer (per capita annual household income ≥16,000 yuan: 59.3% vs 19.9%), and a higher proportion were primiparous (parity=1: 79.2% vs 53.1%). Their first ANC visits were earlier (≤12 weeks: 87.4% vs 83.5%), and they had more ANC visits (≥5 visit: 78.3% vs 65.2%). A lower proportion of women in urban areas suffered from second-hand smoke exposure (17.1% vs 24.3%) and anaemia during pregnancy (11.5% vs 15.6%). Additionally, they were more likely to intake nutrient (IFA: 9.6% vs 4.1%; FA: 69.3% vs 62.8%), and these differences were statistically significant.

Table 2 shows the characteristics of the participants classified by area and nutrient supplementation group. In urban areas, the participants in the three groups differed in terms of childbearing age, maternal education, employment status, per capita annual household income, parity, time of the first ANC visit, number of ANC visits, second-hand smoke exposure and anaemia. In rural areas, the three groups differed in terms of the neonatal sex proportion, childbearing age, maternal education, employment status, parity, time of the first ANC visit, number of ANC visits, second-hand smoke exposure and anaemia. Therefore, when analysing the relationship between prenatal nutrient supplementation and neonatal birth weight, we ran models that were adjusted step by step for these variables as confounders.

Birth outcomes across the groups in urban and rural areas

The birth outcomes across the groups in two areas were presented in Table 3. The mean birth weight in urban areas was higher than that of rural areas. In terms of nutrient supplementation and delivery method, all differences of mean birth weight between urban and rural areas were statistically significant. The proportion of low birth weight (LBW) in urban areas was 2.5%, which was significantly lower than 3.6% in rural areas. For the FA and natural childbirth group, the differences in the proportion of LBW between urban and rural areas were statistically significant.

Association between birth weight and prenatal nutrient supplementation in urban and rural areas

Table 4 presents the mean differences from the 2-level model analysis in urban areas. The association between prenatal nutrient supplementation and neonatal birth weight was not statistically significant from Model 1 to Model 5. We found that the male neonates, mothers worked and 5 or more ANC visits were associated with increased neonatal birth weight. However, gestational age less than 37 weeks, primiparous women (parity=1) and gestational hypertension were associated with decreased neonatal birth weight.

Table 5 presents the mean differences from the 2-level model analysis in rural areas. In the unadjusted model, prenatal IFA supplementation was associated with a 66.5 g (34.2 to 98.8 g) increase in neonatal birth weight, and FA supplementation was associated with a 41.6 g (28.1 to 55.0 g) increase in neonatal birth weight. The significant association was robust when additional adjustments were performed. After adjusting for all covariates, prenatal IFA and FA supplementation increased the mean birth weights by 45.3 g (9.4 to 81.1 g) and 30.9 g (15.6 to 46.1 g), respectively, compared with non-users (Model 5, Table 5). Besides prenatal IFA or FA supplementation, we also found that the male neonates, mothers of higher educational level, better economic status and 5 or more ANC visits were associated with increased neonatal birth weight. While gestational age less than 37 weeks, childbearing age of below 20 years old, primiparous women and gestational hypertension were associated with decreased neonatal birth weight.

DISCUSSION

Main findings

The major finding of this study is that the effects of prenatal IFA and FA supplementation on neonatal birth weights were different between urban and rural areas of Northwest China. In urban areas, prenatal nutrient supplementation was not associated with neonatal birth weights. However, in rural areas, prenatal IFA and FA supplementation increased the neonatal birth weights by 45.3 g (9.4 to 81.1 g) and 30.9 g (15.6 to 46.1 g), respectively.

Comparison with other studies

To the best of our knowledge, there are few reports describing the differences in the effects of prenatal nutrient supplementation on neonatal birth weights between urban and rural areas in China. However, there is still some evidence from studies conducted in different areas showing the different effects of prenatal IFA or FA supplementation on birth weights. For urban areas, a cohort study conducted in the city of Valencia, Spain showed that there was no significant difference in the mean birth weights of children of women who consumed FA and those who did not.[16] Similarly, one study conducted in the New England region of the USA reported that there was no association between FA supplementation and low birth weights.[8] In contrast, a prospective cohort study from the Netherlands showed that pre-conception FA supplementation significantly increased the mean birth weight by 68 g (37.2 to 99.0 g) compared with non-users.[7] In terms of rural areas, a pilot intervention study conducted in 4 rural areas of Vietnam showed that prenatal IFA supplementation increased the mean birth weight by 124 g (68 to 255 g, $p<0.001$).[17] Another study in India found that prenatal IFA supplementation did not have an effect on mean birth weight compared with non-users after adjusting for the number of ANC visits.[6]

The explanation for this finding could be the different nutritional status of pregnant women in urban and rural areas. Consistently with our present study, previous studies have generally reported that mothers of higher educational level, mothers worked, better economic status and adequate ANC visits were associated with increased neonatal birth weights.[18-22] While gestational age less than 37 weeks, childbearing age of below 20 years old, primiparous women and gestational hypertension were negatively associated with neonatal birth weight.[23-25] Besides that, maternal nutrition is the major factors that alter neonatal birth weight.[26] Adequacy of nutrient intakes during preg-

Table 2. Characteristics of participants by areas and nutrient supplementation groups†

Characteristics	Urban				Rural			
	IFA (n=550)	FA (n=3,981)	Non-users (n=1,211)	*p*-value‡	IFA (n=902)	FA (n=13,711)	Non-users (n=7,234)	*p*-value‡
Neonatal characteristics								
Neonatal sex, n (%)				0.196				<0.001
Boy	276 (50.2)	2,086 (52.4)	661 (54.6)		512 (56.8)	7,385 (53.9)	4,080 (56.4)	
Girl	274 (49.8)	1,895 (47.6)	550 (45.4)		390 (43.2)	6,326 (46.1)	3,154 (43.6)	
Gestational age, n (%)				0.780				0.232
<37 weeks	14 (2.6)	123 (3.1)	36 (3.0)		29 (3.2)	355 (2.6)	212 (2.9)	
≥37 weeks	536 (97.4)	3,858 (96.9)	1,175 (97.0)		873 (96.8)	13,356 (97.4)	7,022 (97.1)	
Socio-demographic characteristics								
Childbearing age, n (%)				<0.001				<0.001
<20 years old	3 (0.6)	20 (0.5)	32 (2.6)		15 (1.7)	329 (2.4)	293 (4.1)	
20-34 years old	507 (92.2)	3,641 (91.5)	1,043 (86.1)		813 (90.1)	12,312 (89.8)	6,100 (84.3)	
≥35 years old	35 (6.4)	234 (5.9)	100 (8.3)		65 (7.2)	907 (6.6)	717 (9.9)	
Marital status, n (%)				0.874				0.695
Married	543 (98.7)	3,921 (98.5)	1,192 (98.7)		877 (97.3)	13,376 (97.8)	7,056 (97.7)	
Other	7 (1.3)	59 (1.5)	16 (1.3)		24 (2.7)	308 (2.2)	169 (2.3)	
Maternal education, n (%)				<0.001				<0.001
Primary school or lower	3 (0.6)	63 (1.6)	115 (9.5)		41 (4.6)	1,438 (10.5)	1,619 (22.4)	
Secondary school	36 (6.6)	610 (15.3)	413 (34.1)		450 (49.9)	7,864 (57.5)	4,286 (59.3)	
Senior school or higher	511 (92.9)	3,304 (83.1)	682 (56.4)		411 (45.6)	4,377 (32.0)	1,317 (18.2)	
Maternal employment status, n (%)				<0.001				<0.001
Employed	421 (77.1)	2,785 (70.3)	616 (52.5)		291 (32.4)	3,689 (27.1)	1,602 (22.3)	
Unemployed	125 (22.9)	1,179 (29.7)	581 (48.5)		606 (67.6)	9,949 (72.9)	5,580 (77.7)	
Per capita annual household income, n (%)				<0.001				0.251
<8,000 yuan	24 (4.4)	214 (5.4)	94 (7.8)		261 (28.9)	4,312 (31.5)	2,293 (31.7)	
8,000-15,999 yuan	100 (18.2)	896 (22.5)	354 (29.2)		282 (31.3)	4,206 (30.7)	2,313 (32.0)	
≥16,000 yuan	357 (64.9)	2,439 (61.3)	606 (50.0)		201 (22.3)	2,693 (19.6)	1,455 (20.1)	
Reproductive history								
Parity, n (%)				<0.001				<0.001
1	494 (89.8)	3,334 (83.8)	756 (62.4)		562 (62.3)	7,977 (58.2)	3,205 (44.3)	
≥2	56 (10.2)	647 (16.2)	455 (37.6)		340 (37.7)	5,734 (41.8)	4,029 (55.7)	

ANC: antenatal care; FA: folic acid; IFA: iron plus folic acid.
†Values are presented as n (%) for these categorical variables.
‡*p* values for differences between groups were derived from the chi-square test for categorical variables.

Table 2. Characteristics of participants by areas and nutrient supplementation groups† (cont.)

Characteristics	Urban				Rural			
	IFA (n=550)	FA (n=3,981)	Non-users (n=1,211)	*p*-value‡	IFA (n=902)	FA (n=13,711)	Non-users (n=7,234)	*p*-value‡
Healthcare utilization								
Time of the first ANC visit, n (%)				<0.001				<0.001
≤12 weeks	505 (91.8)	3,575 (89.8)	940 (77.6)		798 (88.5)	12,004 (87.6)	5,430 (21.9)	
>12 weeks	40 (7.3)	369 (9.3)	225 (18.6)		79 (8.8)	1,466 (10.7)	1,584 (75.1)	
Number of ANC visit, n (%)				<0.001				<0.001
<5	44 (8.0)	634 (15.9)	458 (37.8)		144 (16.0)	3,679 (26.8)	3,453 (47.7)	
≥5	501 (91.1)	3,293 (82.7)	700 (57.8)		748 (82.9)	9,886 (72.1)	3,618 (50.0)	
Lifestyles								
Second-hand smoke exposure, n (%)				<0.001				<0.001
Yes	72 (13.2)	634 (16.1)	275 (23.1)		161 (18.1)	2,941 (22.0)	2,195 (31.1)	
No	475 (86.8)	3,309 (83.9)	915 (76.9)		728 (81.9)	10,441 (78.0)	4,858 (68.9)	
Health status								
Gestational hypertension, n (%)				0.321				0.257
Yes	10 (1.8)	79 (2.0)	16 (1.3)		13 (1.4)	220 (1.6)	95 (1.3)	
No	540 (98.2)	3,897 (98.0)	1,193 (98.7)		889 (98.6)	13,475 (98.4	7,124 (98.7)	
Anaemia, n (%)				<0.001				<0.001
Yes	140 (25.5)	423 (10.7)	98 (8.1)		312 (34.6)	2,145 (15.7)	941 (13.1)	
No	409 (74.5)	3,548 (89.3)	1,109 (91.9)		590 (65.4)	11,538 (84.3)	6,266 (86.9)	

ANC: antenatal care; FA: folic acid; IFA: iron plus folic acid.
†Values are presented as n (%) for these categorical variables.
‡*p* values for differences between groups were derived from the chi-square test for categorical variables.

Table 3. Birth outcomes across the groups by urban and rural area

	Urban	Rural	*p*-value†
Birthweight, g, mean (SD)	3,334 (465)	3,249 (453)	<0.001
Nutrient supplementation, g, mean (SD)			
IFA	3,362 (450)	3,298 (441)	<0.001
FA	3,340 (468)	3,262 (445)	<0.001
Non-users	3,303 (463)	3,218 (467)	<0.001
Delivery method, g, mean (SD)			
Cesarean section	3,392 (499)	3,301 (482)	<0.001
Natural childbirth	3,288 (431)	3,225 (436)	<0.001
Low birth weight, n (%)	144 (2.5)	792 (3.6)	<0.001
Nutrient supplementation, n (%)			
IFA	11 (2.0)	28 (3.1)	0.207
FA	92 (2.3)	442 (3.2)	0.003
Non-users	41 (3.4)	322 (4.5)	0.091
Delivery method, n (%)			
Cesarean section	74 (2.9)	253 (3.7)	0.057
Natural childbirth	69 (2.2)	528 (3.6)	<0.001

FA: folic acid; IFA: iron plus folic acid.
†*p* values for differences between two areas were derived from the t test for continuous variable or the chi-square test for categorical variables.

nancy can increase the neonatal birth weight.[27] Previous literature in China suggested that pregnant women in urban areas had significantly higher reference nutrient intake (RNI) fulfilment levels for pregnancy such as Fe and energy comparing with those in rural areas.[12] Our pervious study showed that the majority women in rural areas of Shaanxi Province had low intake of iron and folate which were essential for pregnancy. Our recent study indicated that the pregnant women in urban areas had higher level of folate, Fe, energy, protein and other nutrients.[28] In this study, the neonatal birth weight in urban areas was significantly higher than those in rural areas which indicated that the nutritional status of pregnant women in urban areas might be better.

On the other hand, pregnant women in urban areas with a higher proportion of IFA or FA intake might have a much better nutritional status because of their more concern about nutrition and more likely to have healthier behaviours such as attending ANC visits. Attending ANC visit during the first trimester increased the odds of taking iron supplementation during pregnancy.[29] Studies indicated that the level of folate and other vitamin was significantly lower in women exposed to smoke during pregnancy.[30] Anaemia during pregnancy is a signal of iron deficiency with serious consequences for both mothers and fetus.[31] In our present study, compared with women in rural areas, pregnant women in urban areas started their first ANC visits earlier, had more ANC visits, were less likely exposed to second-hand smoke and suffered from anaemia.

Nutritional status was also associated with sociodemographic characteristics. According to previous studies, a childbearing age of below 20 years old or above 35 years old was a risk factor for folate deficiency.[32,33] Women who had higher educational level and better economic status were more likely to get a higher diet diversity scores and use iron and folic acid.[34,35] More micronutrient deficiencies have been observed in unmarried and unemployed women.[36,37] On the contrary, married women had a greater compliance of using iron supplementation.[38] In this study, we found that the proportion of women of childbearing age (between 20-34 years old) was higher in urban areas, and they were well educated. A higher proportion was married, and they were more likely to be employed and rich compared with women in rural areas.

In general, pregnant women in urban areas had more factors that lead to better nutritional status such as a higher proportion of women of childbearing age (20-34 years old), more education, a higher proportion of married women, higher employment, higher incomes, adequate ANC visits, lower exposure to second-hand smoke exposure and a lower proportion of women suffering from anaemia during pregnancy. Therefore, in urban areas, the benefit of prenatal IFA and FA supplementation on birth weight might be masked by the relatively better nutritional status of pregnant women. Further prospective studies with better designs and large population are needed to explore the association of prenatal nutrient supplementation with birth weight in urban areas. While for rural areas, owing to the relatively poor nutritional status, prenatal IFA and FA supplementation still increased the neonatal birth weights even when controlling for these confounders.

Strengths and limitations

There were several strengths of our study. First, this study used a stratified multistage random sampling method, which made the sample more representative of the Shaanxi Province. Moreover, 27,589 single live births that accounted for approximately 9% of the neonates born in the Shaanxi Province were enrolled. It was a large-scale study, and our findings reflected the effects of prenatal nutrient supplementation in the Shaanxi Province and even Northwest China. Secondly, unlike OLS Regression, which ignores the homogeneity of neonatal birth weights within areas, the multilevel model was an appropriate method for analysing data with a hierarchical structure.

Our study also had some limitations. First, this was a cross-sectional study design, and it was difficult to draw the causal relationship interpretation. Second, although the neonatal birth weights were obtained from the birth

Table 4. Association between birth weight and prenatal nutrient supplementation in urban areas

	Model 1†			Model 2‡			Model 3§			Model 4¶			Model 5††		
	Diff	95% CI	*p*-value‡‡	Diff	95% CI	*p*-value‡‡	Diff	95% CI	*p*-value‡‡	Diff	95% CI	*p*-value‡‡	Diff	95% CI	*p*-value‡‡
Nutrient supplementation															
IFA	41.1	-8.2, 90.4	0.100	49.6	-3.0, 102	0.064	37.2	-16.3, 90.8	0.169	34.2	-19.5, 87.9	0.207	22.3	-31.9, 76.5	0.413
FA	28.0	-3.2, 59.3	0.078	29.0	-5.2, 63.2	0.094	17.5	-17.8, 52.8	0.324	17.0	-18.6, 52.6	0.342	14.7	-20.9, 50.3	0.410
Non-users	Ref	-	-	Ref	-	-	Ref	-	-	Ref	-	-	Ref	-	-
Sex, male				127	102, 152	<0.001	130	105, 155	<0.001	130	104, 155	<0.001	130	105, 156	<0.001
Gestational age, <37 weeks				-572	-706, -438	<0.001	-586	-722, -451	<0.001	-557	-693, -420	<0.001	-553	-689, -417	<0.001
Childbearing age															
<20 years old				-34.1	-168, 99.7	0.610	-35.3	-169, 98.5	0.597	-27.2	-162, 108	0.686	-25.4	-160, 109	0.706
≥35 years old				-25.7	-81.2, 29.9	0.357	-29.8	-85.7, 26.2	0.290	-25.9	-82.1, 30.4	0.360	-23.8	-80.0, 32.5	0.399
20-34 years old				Ref	-	-	Ref	-	-	Ref	-	-	Ref	-	-
Married				54.9	-51.8, 162	0.313	57.7	-49.7, 165	0.292	57.9	-50.1, 166	0.293	62.8	-45.1, 171	0.254
Maternal education															
Senior school or higher				60.8	-17.6, 139	0.125	53.8	-25.8, 133	0.181	49.3	-31.0, 130	0.223	48.0	-32.4, 128	0.236
Secondary school				22.5	-55.2, 100	0.563	15.9	-62.6, 94.4	0.686	11.5	-67.8, 90.7	0.773	8.4	-71.0, 87.8	0.832
Primary school or lower				Ref	-	-	Ref	-	-	Ref	-	-	Ref	-	-
Employed				39.6	9.7, 69.4	0.009	39.5	9.4, 69.7	0.010	40.6	10.3, 70.9	0.009	42.0	11.7, 72.3	0.007
Per capita annual household income															
≥16,000 yuan				39.7	-15.0, 94.3	0.152	45.6	-10.0, 101	0.106	47.7	-8.1, 103	0.093	44.7	-11.3, 101	0.115
8,000-15,999 yuan				28.0	-28.3, 84.3	0.323	35.1	-22.3, 92.4	0.226	37.6	-19.9, 95.0	0.196	35.9	-21.8, 93.6	0.217
<8,000 yuan				Ref	-	-	Ref	-	-	Ref	-	-	Ref	-	-
Parity=1				-59.0	-94.5, -23.4	0.001	-62.4	-98.4, -26.4	0.001	-64.9	-101, -28.7	<0.001	-66.7	-103, -30.5	<0.001
Time of the first ANC visit, ≤12 weeks							-9.9	-51.5, 31.6	0.639	-12.6	-54.3, 29.1	0.555	-11.7	-53.4, 29.9	0.581
Number of ANC visit, ≥5							49.4	14.6, 84.2	0.005	49.3	14.4, 84.2	0.006	49.6	14.6, 84.5	0.005
Exposed to second-hand smoke										-18.8	-52.9, 15.3	0.280	-19.0	-53.1, 15.1	0.275
Gestational hypertension													-113	-207, -19.4	0.018
Anaemia													8.8	-31.5, 49.2	0.668

FA: folic acid; IFA: iron plus folic acid; Diff: difference.
†Model 1: unadjusted model.
‡Model 2: adjusted for social characteristics including neonatal sex, gestational age, maternal childbearing age, marital status, education, employment, per capita annual household income and parity.
§Model 3: adjusted for all variables in Model 2 plus health care utilization, including time of the first ANC visit and number of ANC visits.
¶Model 4: adjusted for all variables in Model 3 plus prenatal lifestyle, including second-hand smoke exposure.
††Model 5: adjusted for all variables in Model 4 plus health conditions during pregnancy, including gestational hypertension and anaemia in pregnancy.
‡‡*p* values were derived from the multilevel model analysis.

Table 5. Association between birth weight and prenatal nutrients supplementation in rural area

	Model 1†			Model 2‡			Model 3§			Model 4¶			Model 5††		
	Diff	95% CI	p-value‡‡	Diff	95% CI	p-value‡‡	Diff	95% CI	p-value‡‡	Diff	95% CI	p-value‡‡	Diff	95% CI	p-value‡‡
Nutrient supplementation															
IFA	66.5	34.2, 98.8	<0.001	61.0	26.1, 95.8	<0.001	49.6	14.2, 85.1	0.007	46.0	10.3, 81.7	0.013	45.3	9.4, 81.1	0.014
FA	41.6	28.1, 55.0	<0.001	39.1	24.4, 53.8	<0.001	32.7	17.6, 47.7	<0.001	30.8	15.5, 46.0	<0.001	30.9	15.6, 46.1	<0.001
Non-users	Ref	-	-	Ref	-	-	Ref	-	-	Ref	-	-	Ref	-	-
Sex, male				121	108, 134	<0.001	122	109, 135	<0.001	124	111, 137	<0.001	124	111, 137	<0.001
Gestational age, <37 weeks				-585	-684, -486	<0.001	-587	-685, -490	<0.001	-589	-686, -491	<0.001	-580	-675, -484	<0.001
Childbearing age, years															
<20				-74.0	-113, -35.2	<0.001	-66.7	-106, -27.5	0.001	-67.1	-107, -27.5	0.001	-67.8	-107, -28.1	0.001
≥35				-26.1	-51.5, -0.6	0.045	-21.0	-46.7, 4.8	0.108	-20.5	-46.5, 5.6	0.121	-17.2	-43.3, 8.8	0.191
20-34				Ref	-	-	Ref	-	-	Ref	-	-	Ref	-	-
Married				-43.8	-87.1, -0.4	0.048	-43.9	-87.7, -0.1	0.050	-40.0	-84.5, 4.4	0.077	-42.2	-86.7, 2.3	0.063
Maternal education															
Senior school or higher				68.8	45.0, 92.6	<0.001	62.4	38.2, 86.6	<0.001	64.6	40.1, 89.0	<0.001	63.7	39.2, 88.2	<0.001
Secondary school				54.9	34.9, 74.8	<0.001	49.9	29.6, 70.2	<0.001	51.4	30.9, 71.9	<0.001	50.2	29.7, 70.7	<0.001
Primary school or lower				Ref	-	-	Ref	-	-	Ref	-	-	Ref	-	-
Employed				15.2	-0.7, 31.1	0.061	13.9	-2.3, 29.9	0.092	11.9	-4.4, 28.1	0.152	11.4	-4.9, 27.6	0.171
Per capita annual household income															
≥16,000 yuan				39.1	20.7, 57.5	<0.001	35.5	16.9, 54.1	<0.001	35.4	16.7, 54.2	<0.001	34.9	16.1, 53.6	<0.001
8,000-15,999 yuan				12.7	-2.6, 28.0	0.102	11.7	-3.8, 27.2	0.135	12.1	-3.5, 27.8	0.125	12.4	-3.2, 28.0	0.117
<8,000 yuan				Ref	-	-	Ref	-	-	Ref	-	-	Ref	-	-
Parity=1				-45.2	-59.5, -31.0	<0.001	-49.2	-63.6, -34.7	<0.001	-47.5	-62.1, -32.9	<0.001	-47.8	-62.5, -33.2	<0.001
Time of the first ANC visit, ≤12 weeks							12.2	-7.0, 31.5	0.212	7.4	-12.0, 26.8	0.456	7.8	-11.6, 27.3	0.429
Number of ANC visit, ≥5							46.9	31.4, 62.5	<0.001	46.0	30.3, 61.7	<0.001	47.0	31.3, 62.7	<0.001
Exposed to second-hand smoke										-6.3	-21.5, 9.0	0.422	-6.4	-21.7, 8.9	0.411
Gestational hypertension													-156	-209, -104	<0.001
Anaemia													1.8	-16.3, 20.0	0.843

FA: folic acid; IFA: iron plus folic acid; Diff: difference.
†Model 1: unadjusted model.
‡Model 2: adjusted for social characteristics including neonatal sex, gestational age, maternal childbearing age, marital status, education, employment, per capita annual household income and parity.
§Model 3: adjusted for all variables in Model 2 plus health care utilization, including time of the first ANC visit and number of ANC visits.
¶Model 4: adjusted for all variables in Model 3 plus prenatal lifestyle, including second-hand smoke exposure.
††Model 5: adjusted for all variables in Model 4 plus health conditions during pregnancy, including gestational hypertension and anaemia in pregnancy.
‡‡*p* values were derived from the multilevel model analysis.

certificates, the information of nutrient supplementation and other variables were self-reported. This may have caused a certain degree of response bias, although it would not have differed among the IFA, FA and non-user groups. Previous studies suggested a high sensitivity for self-reported nutrient supplementation and events in pregnancy.[39-42] Despite this, we cannot rule out the possibility of the misclassification. To minimize the response bias, the survey was tested in a pilot study. Before the formal investigation, all the interviewers received uniform training according to detailed interviewer guides. Furthermore, we use a standardized questionnaire to collect the information for the investigation, as well as detailed supporting materials such as images of nutrient supplements and calendars. Third, we lacked data on the dosages and frequencies of prenatal nutrient supplementation, which limited us to find possible factors that may explain the different effects of prenatal nutrient supplementation between urban and rural areas. Fourth, although the common inadequate intake of iron and folate from dietary among pregnant women in both urban and rural areas of Shaanxi Province, the interpretation of our findings was limited by lack of information on the extent of iron and folate based on dietary intake. Fifth, we adjusted for potential confounders including social-demographic characteristics, healthcare utilization, lifestyles and health conditions during pregnancy. However, in nutrient supplement studies, residual confounders and other unobservable factors are always of concern. Our findings would be much stronger if we had considered the maternal pre-pregnancy body mass index, gestational weight gain, and iron and folate biomarkers. Nevertheless, as an exploratory study, the results are still credible considering the large total sample size.

Conclusions

The effects of prenatal nutrient supplementation on neonatal birth weights differ between urban and rural areas of Northwest China. Prenatal IFA and FA supplementation seems to have no significant effects on the birth weights of neonates born to women in urban areas. In rural areas, however, prenatal IFA and FA supplementation can significantly increase neonatal birth weights. The different effects may be due to the different nutritional status of pregnant women in urban and rural areas of Northwest China. Our findings suggested the nutritional status of pregnant women in rural areas was relatively poor and prenatal nutrient supplementation may be a helpful way for improving neonatal birth weight in rural areas of Shaanxi Province of Northwest China.

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AUTHOR DISCLOSURES

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