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The association between prenatal micronutrient supplementation and early development of children under age two: Evidence from rural Guizhou, China

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ABSTRACT

Background: Maternal nutrition has been shown to positively impact the pregnancy outcomes of women, as demonstrated by a decreased rate of infants born with below-average weight and size for gestational age. However, current evidences supporting the association between prenatal micronutrient supplementation and the early development of children is limited and mixed.

Aims: This study investigates the association between prenatal micronutrient supplementation and the development of children under age two in rural area of Guizhou province, China.

Methods: We interviewed the primary caregivers of 446 children 6–24 months old in the study area. Based on the caregivers' self-reported information about micronutrient supplementation of the child's mother during pregnancy, we divided their children into the supplemented group and the non-supplemented group. The interviews also collected sociodemographic information about the mother, the child, other family members and the households. We used the Bayley Scales of Infant Development III (BSID-III) to measure children's cognitive, language, motor, and socioemotional abilities and employed a multivariate linear regression model adjusted for confounding variables to estimate the association of interest.

Results: Our data shows that 33.4% of mothers received micronutrient supplementation during pregnancy. Children in the supplemented-group had significantly higher mean scores in language (3.27; 95% CI: 0.42–6.13; $p = 0.03$) domain compared to children in the non-supplemented group.

Conclusion: This study provides additional evidence for the association between prenatal micronutrient supplementation and improved language development of rural children in the first two years of life. The conclusion is of certain value to the local and even national policy makers.

1. Introduction

A great number of pregnant women worldwide either have limited access to sufficient nutrition or are not aware of the importance of nutrition in meeting the metabolic and physiologic demands of pregnancy (Battalwar & Agarwal, 2015; Panwar & Punia, 1998). Research shows that the worldwide prenatal iron deficiency anemia is 15–20%; iodine deficiency ranges from 17% in Oceania to 40% in Africa (Gernand, Schulze, Stewart, West, & Christian, 2016). Since fetal metabolic demands increase as gestational age increase, pregnant women should take a nutritional diet during the course of gestation to increase the chance of having a healthy pregnancy outcome (Shah & Ohlsson, 2009). This is of particular importance, given the fact that the intrauterine environment not only plays a pivotal role in fetal development but also has the potential to result in lasting health effects on offspring (Schlotz & Phillips, 2009).

Over the past forty years since the Reform and Opening-up, the nutritional condition in China and some of the nutritional supplementation habits of Chinese people, including women of childbearing age, have significantly improved (Yin & Dong, 2018). The rate of folic acid supplementation among mothers during pregnancy increased from 20.5% in 2002 to 49.9% in 2009 (Wang et al., 2011). However, the uptake rate of iron, zinc, and vitamin supplementation of the same population remained less than 20% (Wang et al., 2011). Micronutrient deficiency, especially vitamin D deficiency, is still prevalent among pregnant women in rural China (87.42%),with a significant difference between average rural areas and poor rural areas (Wang et al., 2011). A survey was conducted in three provinces of China in 2011, showing that the overall prevalence of anemia among pregnant women in these provinces was 23.6%, which means that 1 in every 4–5 pregnant women has anemia (Meng, Zhang, & Hou, 2011).

Maternal nutrition has been proved to have a direct impact on the

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growth of the fetus; yet the effect of micronutrient supplementation during pregnancy on children's neurodevelopment remains debatable and unclear. Some empirical studies, including a meta-analysis, found that maternal nutrition interventions had insignificant effects on neurodevelopment of children (Hamadani, Fuchs, Osendarp, Huda, & Grantham-Mcgregor, 2002; Larson & Yousafzai, 2015; Schmidt, Siti, West, Werner, & Hautvast, 2004; Tofail et al., 2008). Another recent meta-analysis found a small pooled effect of maternal nutritional supplementation intervention on both physical growth, including LAZ or HAZ, and neurodevelopment, including the cognitive, language, motor, and social-emotional development of children (Prado, Larson, & Cox, 2019). However, some studies indicated that prenatal micronutrient supplementation impacts not only infants' and young children's physical health, which includes birth outcomes and fetal growth (Haider & Bhutta, 2006; Shah & Ohlsson, 2009), but also their psychological development, which includes cognitive development (Li et al., 2009), language development (Christine et al., 2011; Villamor, Rifas-Shiman, Gillman, & Oken, 2012), motor development (Joos, Pollitt, Mueller, & Albright, 1983; McGrath et al., 2006; Villamor et al., 2012), and behavioral development (Roza et al., 2010; Villamor et al., 2012).

Although several studies explored the prenatal micronutrient supplementation and its association with early development of children in China, their results are neither comprehensive nor consistent. Zhu et al. (2018) revealed a positive association between prenatal micronutrient supplementation and the mental development of children (Zhu et al., 2018). A study on a cohort of infants at 3, 6, and 12 months of age concluded the positive effects appears only in the psychomotor development of 1-year-old infants but not in the mental development among children aged 3–6 months (Li et al., 2009). An earlier study conducted in rural Taiwan, with prenatal micronutrient supplements as an independent variable, found that motor scores of 8-month-old infants in the treatment group were significantly higher than those in control groups, while no effect was revealed in terms of the mental development of the sample children (Joos et al., 1983).

Our analytical framework for the analysis of prenatal micronutrient supplementation and early child development is grounded in a series of related studies. The theory of fetal programming states that maternal nutritional status and the uterine environment begin operating in the early stages of development and determine the metabolic and endocrine events that are crucial to normal growth and development of the fetus (Baker, 1995). The micronutrients supplemented during pregnancy play critical roles in the cellular metabolism, development, and maintenance of normal functioning of the mother (Haider & Bhutta, 2006). Changes in the fetal environment during sensitive periods of organ development may cause crucial changes in the structure and functioning of these organs later in life, offering greater chances for healthy mental health development of children (Schlotz & Phillips, 2009).

In this paper, we aim to provide additional evidence for the association between prenatal micronutrient supplementation and the early development of children under two years old in the rural area of Guizhou province, a typical underdeveloped province in the western China (Bureau, 2017).

2. Materials and methods

2.1. Participants

The cross-sectional study was conducted in a township in the northwestern part of Guizhou province. Guizhou is a relatively poor province in southwestern part of China and ranks 29 out of 34 provinces nationally in terms of per capita GDP in the year 2016. To identify the sample, we first used government statistics to compile a list of townships in the county, and then selected the sample township that is representative in terms of per capita GDP (Bureau, 2017). The sample township has nine administrative villages with a population nearly 30,000.

We calculated the target sample size to detect a 0.35 standardized effect on Bayley-III scores. We assumed an adjusted intraclass correlation coefficient (ICC) of 0.1, with a coefficient of variation of cluster sizes of 0.5. Based on these parameters, we required 41 clusters (in this case, 41 settlements) to detect an effect size of 0.35 SD at 80% power given a two-sided significance level of 0.05. Results from power calculations show that the minimum requirement of sample size is 410 children.

For each sample village, we obtained a list of registered births from the local family planning official. All the 582 children aged 6–24 months at the time of data collection in the 41 settlements constitute our sampling frame. Of those 582 children, 111 had migrated to other places with their parents, and 25 did not complete the initial interview. Therefore, this study involves 446 children.

The Peking University Institutional Review Board (PU IRB), Beijing, China, approved the ethical assessment of the study (No. IRB00001052-17056). The purpose of the study was explained and verbal informed consent was obtained from the parents or guardians of all of the children.

2.2. Data collection

We visited eligible households to collect the following data during a three-week home-visit interview: household demographic and socioeconomic status, test scores on the cognitive, language, motor, and socioemotional development of children, the feeding behavior of children, and whether the mothers supplemented micronutrient during pregnancy.

We trained 39 college students as enumerators who were blind to study hypotheses to administer the development assessments of sample child, and interview the child's primary caregiver who takes primary responsibility for the child's daily care. The 39 enumerators were divided into two groups: one group of 15 enumerators were trained through a step-by-step process to build proficiency in a BSID test, and another group of 24 enumerators were trained in obtaining demographics, SES, and on feeding behaviors. Both groups were trained intensively for one week, specifically, eight hours per day for seven consecutive days to make sure that they understand the survey in a consistent way and can administer the survey in a standardized way.

The training specialists have years of experience conducting field survey and quantitative analysis. They delivered training sessions through multiple instructional techniques such as lectures on theoretical background to the scale, group discussions about how to optimize the setting for administration, hands-on examples, and on-site practices. As a part of the standardized training procedures, enumerators were required to pass an inter-rater reliability exercise, which aims to ensure different enumerators give consistent evaluation of the same behavior. Each enumerator watches and separately score ten video recordings of actual BSID tests of children aged 6–24 months. Video recordings were made by the training specialists in previous studies. Reliability was analyzed by calculating the ICC for each BSID subscales by age group. ICCs above 0.8 were considered "pass".

A series of measures were taken to ensure quality data collection. First, the team carefully developed the research protocols and questionnaire at the proposal stage. Pretesting around the sample areas were invaluable components of this research, affording the team an opportunity to identify questions that don't make sense to participants, or problems with the questionnaire that might lead to biased answers. Additionally, in a triumph of data collection, crosschecking was conducted at the enumerator level, and routinely special investigations were conducted by the research team. During each step of quality control, the team paid great attention to resolve anomalies, and to ensure that issues were identified and dealt with in a timely fashion.

2.2.1. Socioeconomic status and prenatal micronutrient supplementation

The demographic characteristics and socioeconomic status of sample households were collected during home visits. Information about prenatal micronutrient supplementation of sampled mothers was collected in the structured interview questionnaire, the research team then divided the participants into the supplemented group and the non-supplemented group according to their answers to the supplementation-related question, “Have you (mother of sample child) taken vitamins, minerals, or nutrition tablets at least three times a week in the first three months after discovering that you were pregnant?”

2.2.2. Outcome measures

Neurodevelopment of the sampled children was evaluated based on the Bayley Scales of Infant Development III (BSID-III), an elaborate and comprehensively examined scale with great reliability and validity. The test was taken one-on-one with children interacting with a set of standardized toys and a detailed scoring sheet. BSID-III provides four scales to evaluate the development of child with ages ranging from 0 to 42 months: the cognitive scale, the language scale, the motor scale, and the social-emotional scale. The cognitive scale assesses play skills, information processing (attention to novelty, habituation, memory, and problem–solving), counting, and number skills (Bayley, 2005; Robertson, 2010). The language scale assesses communication skills including language and gestures (Bayley, 2005). The motor scale assesses fine and gross motor skills (Bayley, 2005). The social-emotional scale assesses functional emotional skills, such as self-regulation and the ability to use emotions in a purposeful manner (Bayley, 2005). The cognitive, language, and motor scales evaluate the child’s performance on a series of interactive tasks, whereas the social-emotional scale is based on the caregiver’s responses to a series of questions (Lowe, Erickson, Schrader, & Duncan, 2012). The raw score was calculated as the number of test items that preceded the starting item plus the number of items completed by the child (Bayley, 2005). The composite scores for the cognitive, language, and motor scales are age-standardized with a normative mean (SD) score of 100 (Bos, 2013; Li et al., 2009; Serenius et al., 2013).

Translation, back translation, and cultural adaptation have been conducted for the Chinese version of the harmonized Bayley Scales of Infant Development III to ensure that the four scales of early childhood development would not be overestimated or underestimated under local circumstances (Xu et al., 2011; Yang & Liu, 2016). Internal consistency reliability was tested through Cronbach’s alpha. The results show that the Cronbach’s alpha coefficient was 0. 659–0. 779, which are acceptable with this study’s sample (Nunnally, 1978).

2.2.3. Confounding factors

In addition to the early development of children, we collected data on factors that could confound the association between prenatal micronutrient supplementation and early development of children, which include four categories of variables: (1) child characteristics: gender (boy/girl), age in months (mean ± standard deviation (SD)), low birthweight (yes/no), and height-for-age (mean ± standard deviation (SD)); (2) mother characteristics: age in years and education level (greater than 9 years/at most 9 years); (3) household characteristics: whether the mother is the primary caregiver (yes/no), family income in the last year (greater than 25,000 yuan/at most 25,000 yuan), home parenting environment (mean ± standard deviation (SD)); and (4) feeding behavior: duration of breastfeeding in month (mean ± standard deviation (SD)), and complementary feeding when the child aged 6 months or above (yes/no). To increase the accuracy of estimation, we further controlled these confounding variables in the multivariate linear regression.

In this study, low birth weight is defined as less than 2500 g, and complementary feeding includes any liquid or solid food other than breast milk or adapted formula. The home parenting environment was evaluated based on The Child Care HOME Inventories, which is commonly used to assess the quality of child care and family stimulation. The Cronbach’s alpha coefficient of the HOME inventory fall into a moderate to strong range (α = 0.58–0.84), which demonstrated good internal consistency in our sample (Nunnally, 1978).

Apart from prenatal nutrient supplementation, appropriate breastfeeding and complementary feeding practices are fundamental to children’s nutrition and health outcomes during early stage of life as well (Brown, 2007). We also assessed the potential association between feeding behaviors, including breastfeeding and complementary feeding, and early development of children in all 446 families.

2.3. Statistical analysis

Early development of children as continuous variables were presented as mean ± standard deviation, compared by T-test. Categorical variables were presented as numbers (percent) and compared between the supplemented group and the non-supplemented group using a chi-square test. We performed multivariate linear regression, with cognitive, language, motor and socioemotional development scores as dependent variables in separate analyses and self-reported prenatal micronutrient supplementation as an independent variable. Statistical analyses were performed using Stata 14.2 software. The significance level was set to $p < 0.05$ (2-tailed).

The bivariate linear regression model is as follows:

$$Y_i = \beta_0 + \beta_1 SUPP_i + \epsilon_i \tag{1}$$

where Y_i denotes the development of child i, as measured by BSID-III standardized scores on cognitive, language, motor, and socioemotional developments. $SUPP_i$ is the self-reported micronutrient supplementation during pregnancy of the mother, and ϵ_i is the error term of the model, which is clustered at the natural village level and adjusted for village fixed effect.

The multivariate linear regression model is as follows:

$$Y_i = \beta_0 + \beta_1 SUPP_i + \beta_2 CHILD_i + \beta_3 MOTHER_i + \beta_4 HHS_i + \beta_5 FEEDING_i + \epsilon_i \tag{2}$$

where $CHILD_i$ is a vector of child characteristics, including gender, age in months, and low birth weight; $MOTHER_i$ is a vector of maternal characteristics, including age and level of education; HHS_i is a vector of household characteristics, including whether the mother is the primary caregiver and the family income in the last year. $FEEDING_i$ is a vector of feeding behavior, including having ever breastfed, still breastfeeding or breastfeeding more than 12 months, and complementary feeding when child is aged 6 months or above. The meanings of Y_i, $SUPP_i$, and ϵ_i are the same as those in Eq. (1).

The hypothesis drawn from Eqs. (1) and (2) is that β_1 does not equal zero, indicating that early childhood development is associated with micronutrient supplementation during pregnancy of the mother.

3. Results

According to the self-reported questionnaire, 149 mothers (33.4%) reported to have taken micronutrient supplementation during pregnancy (Table 1), and they tended to have a higher educational level than those of the non-supplemented group. Meanwhile, mothers in the supplemented group were more likely to be the primary caregiver of their children and had higher family incomes in the preceding year compared to those in the non-supplemented group. Yet, there was no significant difference in the mother’s feeding behavior between both groups. Moreover, no significant correlation was found between maternal micronutrient supplementation and the child’s gender, age, and birth weight status.

The density distribution curves of the four BSID-III standardized scores (Fig. 1) leaves us a intuitive sense of the development differences between the treatment group and the control group. The mean of cognitive, language, motor in the supplemented group is larger, whereas the difference on mean of socioemotional score is not obvious.

Table 1
Comparison of child development and socioeconomic characteristics between children with and without maternal nutritional supplementation.

Variables	Maternal nutritional supplementation		*P* value
	No (n = 297)	Yes (n = 149)	
Sex			
Boy	169(56.9)	88 (59.1)	0.66
Girl	128(43.1)	61 (40.9)	
Age of child in month (Mean ± SD)	14.9 ± 5.4	14.1 ± 5.7	0.13
Low birth weight			
No	273 (92.5)	141 (94.1)	0.41
Yes	22 (7.5)	8 (5.9)	
Height-for-age	−0.81 ± 1.24	−0.5 ± 1.25	0.02
Age of mother in year (Mean ± SD)	24.5 ± 5.1	24.8 ± 4.6	0.54
Education of mother			
≤9 years	270 (90.9)	123 (82.6)	0.01
> 9 years	27 (9.1)	26 (17.4)	
Is mother primary caregiver			
No	172 (58.3)	50 (33.6)	< 0.01
Yes	123 (41.7)	99 (66.4)	
Family income in the last year (RMB)			
≤50,000 Yuan	214 (72.1)	93 (62.4)	0.04
> 50,000 Yuan	83 (27.9)	56 (37.6)	
Duration of breastfeeding in month (Mean ± SD)	6.21(5.14)	5.81(4.81)	0.43
Complementary feeding when child aged above 6 months			
No	194 (65.3)	98 (65.8)	0.93
Yes	105 (34.7)	51 (34.2)	
Home parenting environment	24.1 ± 5.2	28.4 ± 4.6	< 0.01

It implies the positive association between having nutritional supplementation during pregnancy and early development in cognitive, language, and motor skills. Through comparing the correlation of BSID-III standardized score and characteristics of sampled children, we found that the cognitive, language and motor test score were themselves related to the child's age (Fig. 2, Panel A, B, and C). As the children aged, their cognitive and language scores decreased, whereas their motor score increased and their socioemotional score remained unchanged.

In addition, we assessed the association between feeding behavior and early development of children (Table 2). We focused on three indicators regarding the feeding behavior: having ever breastfed (yes/no), still breastfeeding or breastfeeding more than 12 months (yes/no), and complementary feeding when child is aged above 6 months (yes/no). We found that children who had been breastfed had higher cognition, language, and motor scores, though the associations were not significant. Still breastfeeding or breastfeeding for more than 12 months had a significantly negative effect on the child's social emotional ability (80.9; 95% CI: 70.3–91.5; p = 0.01 vs. 85.8; 95% CI: 73.8–97.8; p = 0.01). In contrast, cognition scores of children aged above 6 months who had complementary feeding were significantly lower (92.0; 95% CI: 76.1–107.9; p = 0.02 vs. 95.8; 95% CI: 79.4–112.2; p = 0.02).

Table 3 reports the findings of the bivariate and the multivariate linear regression for the association between prenatal micronutrient supplementation and child development (Table 3). The association is positive and significant for children's cognitive, language, and motor scores. After adjusting for potential covariates, the association remains positive and significant only for children's language score (3.27; 95% CI: 0.42–6.13; p = 0.03). Whereas the association between micronutrient supplementation and children's cognitive (2.92; 95% CI: −0.35–6.17; p = 0.08), motor (3.21; 95% CI: −0.36 to 6.78: p = 0.07), and social emotional scores (−0.28; 95% CI: −2.25 to 1.69: p = 0.77) are insignificant. This suggests that the language development of a child in the supplemented group potentially increases by 3.27 points in early childhood, after adjusting for a series of covariates.

4. Discussion

Our study found that 66.6% of mothers in rural Guizhou did not

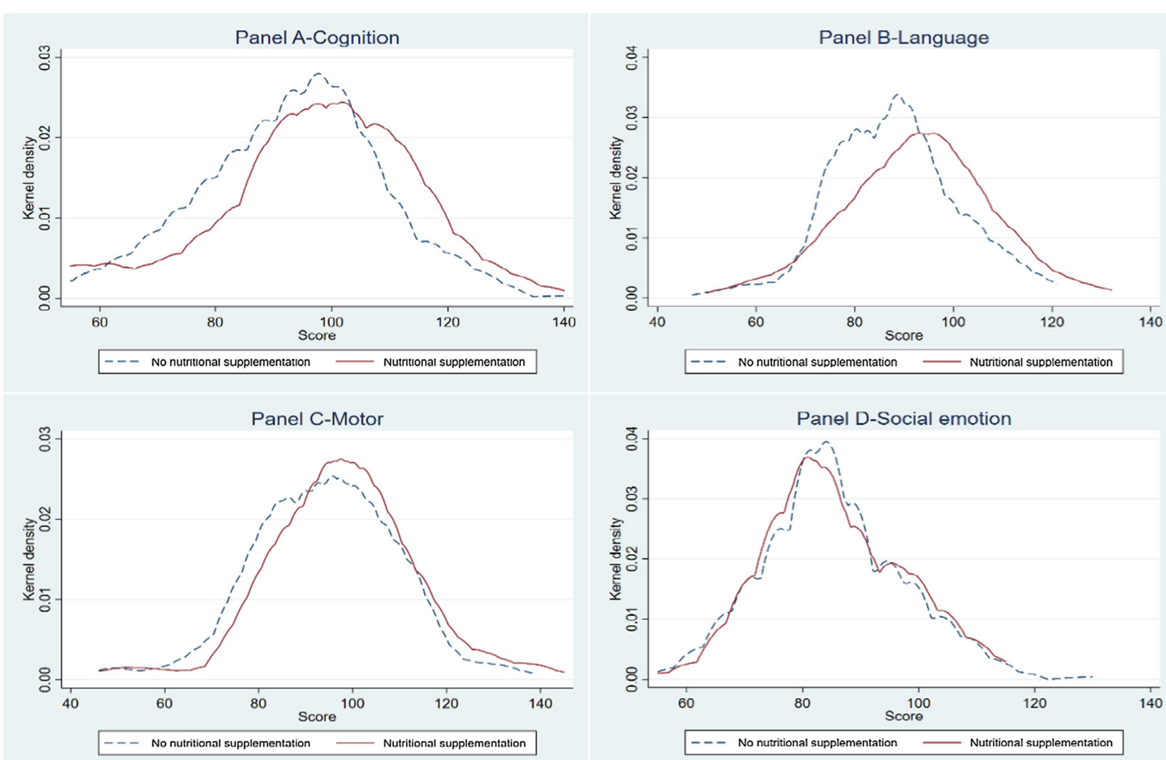

Fig. 1. The density distribution of cognitive score (Panel A), language score (Panel B), motor score (Panel C), and social-emotonal score (Panel D) of the supplemented group and non-supplemented group.

Fig. 2. Early development tendency among sample children.

Table 2
Comparison of child development by feeding behavior of sample children.

Variables	Cognitive score		Language score		Motor score		Socioemotional Score	
	(Mean ± SD)	*P* value	(Mean ± SD)	*P* value	(Mean ± SD)	*P* value	(Mean ± SD)	*P* value
Ever breastfeeding before								
No (95)	94.1 ± 16.5	0.79	87.9 ± 13.6	0.13	94.0 ± 16.2	0.33	86.1 ± 12.2	0.51
Yes (351)	94.6 ± 16.2		90.3 ± 13.7		95.8 ± 15.6		85.2 ± 11.8	
Still breastfeeding or breastfeeding more than 12 months								
No (401)	94.8 ± 16.5	0.22	89.8 ± 13.7	0.76	95.1 ± 15.7	0.24	85.8 ± 12.0	0.01
Yes (45)	91.7 ± 13.9		89.1 ± 15.1		98.0 ± 15.9		80.9 ± 10.6	
Complementary feeding when child aged above 6 months								
No (292)	95.8 ± 16.4	0.02	90.5 ± 13.9	0.11	94.9 ± 15.8	0.36	85.5 ± 11.7	0.59
Yes (154)	92.0 ± 15.9		88.3 ± 13.7		96.3 ± 15.8		84.9 ± 12.3	

SD, Standard deviation. numbers in parenthesis are quantities for categorical variables.

have micronutrient supplementation during pregnancy, even though nutritional interventions during pregnancy have received an increasing amount of public attention from the central government, from the medical system, and from the general public. The Chinese State Council, in major national public health projects, has supplied free folic acid supplementation to pregnant women in early pregnancy in rural China since 2009, with the aim of preventing neural tube defects. However, this study shows that more actions should be taken, as only one-third of the sample of mothers had micronutrient supplementation during pregnancy.

Consistent with previous studies, our results support that maternal micronutrient supplementation during pregnancy has a positive association with language development of children (Christine et al., 2011; Villamor et al., 2012). On the other hand, we found insignificant differences in terms of cognitive, motor, and socioemotional development between supplemented group and non-supplemented group. In a meta-regression of randomized trials done during pregnancy and with children aged 0–5 years, Prado et al. (2019) found a small pooled effect of nutritional supplementation only intervention on the neurodevelopment of children, including cognitive, language, motor, and social-emotional, and a greater pooled effect size of caregiving (parenting) interventions on child development, 4 to 5 times greater than the effect size of nutrient-only intervention (Prado et al., 2019). Beside nutrition, there are several pathways through which socioeconomic status can affect brain and behavioral development of young children, ranging from health care, housing, parenting and cognitively-stimulating play materials to social experiences (Pollak, 2012; Rosales, Reznick, & Zeisel, 2009). That is to say, the development of cognitive, motor, and socioemotional competence requires more comprehensive interventions than merely maternal nutritional supplementation during pregnancy

Table 3
Multivariate analysis for maternal Nutritional supplementation during pregnancy on child development in Guizhou province.

	Unadjusted analysis (Nutritional supplementation during pregnancy = 1)[a]		Adjusted analysis (Nutritional supplementation during pregnancy = 1)[a,b]	
Dependent variables	Coefficient (95% CI)	P value	Coefficient (95% CI)	P value
Cognitive score	4.47 (1.23, 7.70)	0.01	2.92 (−0.35, 6.17)	0.08
Language score	4.85 (2.47, 7.23)	< 0.01	3.27 (0.42, 6.13)	0.03
Motor score	3.82 (0.44, 7.19)	0.03	3.21 (−0.36, 6.78)	0.07
Social emotion score	0.65 (−1.03, 2.32)	0.44	−0.28 (−2.25, 1.69)	0.77

[a] Standard errors are clustered at the natural village level.
[b] Regression estimates from multiple linear models adjusted for gender, age, birth weight, and height-for-age of child, age and education of mother, whether mother is primary caregiver, family income, home parenting environment, duration of breastfeeding in month, complementary feeding when child aged above 6 months, and village fixed effect.

(Luo, Liang, Liu, Zhang, & Yue, 2016).

We found in this study that children who had complementary feeding after 6 months of age received lower cognitive scores, comparing with those who had complementary feeding earlier. There is some published research showing that nutritional status of predominantly breastfed infants younger than 6 months of age was not affected by the consumption of food intake (Thiombiano-Coulibaly, Rocquelin, Eymard-Duvernay, Zougmore, & Traore, 2004). However, their daily nutritional requirements increase as the infants grow rapidly after the first six months, as they need more nutritional intake than the nutrients they can get from breast milk. Hysteretic complementary feeding after 6 months of age would potentially lead to nutritional deficiency, and therefore delays childhood development.

This study also found that cognitive and language scores of the sample children decreased with age. Two risk factors in the parenting environment are possible explanations for the lower cognitive and language scores with age, namely, inadequate nutrients to meet basic requirements for development, as well as the absence of interactive parenting inputs, such as storytelling, reading, singing, and playing. This hypothesis is supported by the findings on *Lancet*, saying that maternal and child undernutrition, and unstimulating household environments, contribute to deficits in children's development and health and productivity in adulthood (Black, Victora, & Walker, 2013). Traditional supplementary food may not be sufficient to meet the nutritional requirements of children above 6 months of age, and can potentially lead to anemia and cognitive delays among these children (Luo et al., 2016). Meanwhile, the subpar parenting practices can lead to developmental delays early in life, which impair child's performance in the long term as they grow up (Wang, Liang, Zhang, Jonsson, & Li, 2019).

This study makes additional contributions to the evidence based on the possible neurocognitive association of prenatal micronutrient supplementation in rural China. To the best of our knowledge, it is the first study to explore the association between prenatal micronutrient supplementation and early childhood development in rural Guizhou, a relatively distant and economically underdeveloped area in China. Even though we excluded those children who had migrated to other places with their parents, this data is still meaningful and representative of contemporary rural China.

This study has several limitations. First, the evaluation of prenatal micronutrient supplementation in the current study relies solely on the self-reported questionnaire. The research team drew information from self-reported questionnaires rather than physiological indicators, such as specific microelements in the blood. Second, several antenatal factors that may influence early development of children were not considered due to certain operational difficulties. The selection bias, such as the existence of non-randomized maternal education and family wealth, were potential sources of bias, which should be address in future study. Third, while our findings are generalizable to the population of women and children in rural Guizhou, they might not be generalizable to women and children who live in rich rural areas along the East Coast of China. Finally, our result only implies correlation rather than causation between prenatal micronutrient supplementation and early development of children given the nature of the cross-sectional design. Further research is needed to better elucidate possible mechanisms.

The nutritional status and their need for supplementation among pregnant women in poor rural China also merit attention. Despite improved maternal iron status in recent years, most women had marginal-to-poor iron status at or near term (Zhao, Xu, & Zhou, 2015). He, Pan, and Yang (He, Pan, & Yang, 2016) showed that, the prevalence of underweight among female in rural China remained a nonnegligible problem in China, and the prevalence is especially significant among adolescents and young women (He et al., 2016). Nevertheless, the proportion of urban pregnant women taking supplements before and during pregnancy was much higher than that of rural pregnant women (Zhang et al., 2018).

Taking into account our findings and their nutritional needs of pregnant women in poor rural China, the potential implications for practice include the need to ensure that pregnant women, especially those who are living in impoverished rural areas, receive sufficient micronutrient supplementation, such as calcium, zinc, iron, vitamin A, vitamin D, or folic acid, during the gestational period based on their own physical needs. Given that some people who are born without the MTHFR enzyme can't convert folic acid into methylfolate, it is recommended to get a physical examination before supplementing folic acid. People with MTHFR 677TT genotypes are supposed to supplement active folic acid, or consume vegetables and fruits to get natural folate instead of folic acid (Yang, Liu, Li, Fan, & Zhi, 2013). Public health interventions, such as free pregnancy nutritional supplementation, and the education of women of childbearing age on the importance of adequate nutrition for the improvement of pregnancy outcomes, should become a priority of the government.

5. Conclusion

This paper offered additional evidence on the severity of delayed neurodevelopment among children aged 0–3 years old in rural China, and the positive association between prenatal micronutrients supplementation and language development of children from low-resource context. However, the effects of prenatal micronutrients on the overall neurodevelopment of child still remains unclear, which calls for further investigation. Considering the lasting effects of maternal nutrition and health on child's performance in the long term, public health interventions, which are designed to raise public awareness and motivation for and provide key access to maternal micronutrient supplementation during pregnancy, are necessary investments in human capital formation in China.

CRediT authorship contribution statement

Yang He: Methodology, Validation, Formal analysis, Writing - original draft, Writing - review & editing. **Jingjing Gao:** Formal analysis, Writing - review & editing, Visualization. **Tianyi Wang:** Software, Project administration, Investigation. **Chengfang Liu:** Writing - review & editing. **Renfu Luo:** Conceptualization, Resources, Writing - review & editing, Supervision, Funding acquisition.

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Appendix A. Supplementary material

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